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TITLE: Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study

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14. ABSTRACT
Purpose: To examine neuropsychological outcomes associated with OIF deployment. Secondary objectives include identification of risk and resiliency factors for adverse neuropsychological outcomes. Scope: Prospective cohort design in which deploying Army soldiers are assessed once prior to deployment and twice after redeployment. A comparison group of soldiers is assessed before and after a period of garrison duty. Methods include administration of performance-based neuropsychological measures and self-report surveys. Progress: Time 1, Time 2, and Time 3 data collection are completed. Analyses of Time 3 data are on-going. Major findings: OIF deployment was associated with neuropsychological abnormalities, including disadvantaged memory and attentional performance, increased emotional distress, and advantaged simple reaction time. Deployment was also associated with increased risk of PTSD, particularly among soldiers reporting greater stress exposures and those activated from NG status. Unit cohesion buffers the adverse effects of early life events on PTSD prior to deployment..

15. SUBJECT TERMS
Deployment health, neuropsychology, cognitive functioning, stress, environmental hazards, Iraq

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INTRODUCTION

Unexplained health symptoms appear to be ubiquitous to modern war.[1] However, questions remain regarding linkages between military operational deployment and the development of physical or mental health symptoms. An area of particular vulnerability may be neuropsychological functioning. For example, following the 1991 Gulf War (GW), significant subsets of military personnel and veterans reported non-specific health (e.g., headache, fatigue) and cognitive (e.g., memory impairment) symptoms suggestive of possible neural dysfunction.[3-7] Neuropsychological functioning encompasses cognitive (e.g., memory, attentional, reasoning), perceptual-sensory-motor (e.g., motor speed), and emotional (e.g., mood) behaviors thought to reflect neural integrity. Unresolved issues include whether subjective neuropsychological complaints correspond to objectively measured indices; whether neuropsychological problems can be linked to specific environmental exposures, stress exposures, or other deployment-related experiences; and the interaction of deployment with potential risk and resilience factors on neuropsychological functioning.

The work encompassed in this report is now referred to as the Neurocognition Deployment Health Study (NDHS). To help address the gaps in knowledge described above, the NDHS incorporates prospective administration of performance-based measures of neuropsychological functioning in cohorts of Army Soldiers deploying in support of Operation Iraqi Freedom (OIF) and in a similar group of Soldiers before and after an interval of non-deployment. The objectives of this ongoing study are to (a) examine the impact of combat-zone deployment on neuropsychological outcomes, including neurobehavioral and emotional functioning, (b) examine the impact of deployment-related stress and environmental exposures on neuropsychological outcomes, and (c) identify potential health risk and protective factors relevant to neuropsychological outcomes. A secondary objective of the study is to describe select psychiatric outcomes, the importance of which is suggested by high rates of PTSD and other psychiatric disorders following Iraq deployment.[2]

BODY

Project History

The original SOW described the following elements within a 24-month timeframe:

<u>YEAR 1</u>	<u>Phase I</u>	
Task 1	Proposal phase and Week 1	Orient project staff to project tasks, training, set-up
Task 2	Months 1-4	Phase I pre-deployment, baseline assessment & data collection, creation of database
Task 3	Months 5-8	Collection of electronic medical/health care record system databases through data requests, transfer of test data to formats readable by statistical software; data entry
Task 4	Months 9-12	Preliminary analyses of Phase I data collection.
<u>YEAR 2</u>	<u>Phase II</u>	
Task 1	Months 1-4	Post-deployment assessment & data collection; collection of electronic deployment-related service information through data requests; data transfer; data entry
Task 2	Months 5-7	Complete collection of electronic deployment-related service information, data transfer, and data file linking of pre- and post- databases.
Task 3	Months 8 – 12	Final data analysis; preparation of reports

The SOW was later approved to extend to a 72-month time frame, the final 24 months of which reflect a no-cost extension. The 72-month time frame reflects in part modifications to the data collection schedule associated with the deployment rotations of the military units included in the study and initial delays in the study associated with administrative approvals and identification of appropriate military units. In addition, it reflects the addition of a third data collection point for each unit so that longitudinal stability may be assessed and outcomes expanded to include health behaviors and occupational functioning. The final 12 month extension reflects the need for additional time to complete data analysis due to administrative interruption secondary to administrative irregularities within LVREC and the transfer of the PIs research laboratory from New Orleans to Boston.

The history of the project is as follows:

Nov 02:	Proposal submitted
Dec 02:	Made contact with US Army Forces Command (FORSCOM) Surgeon's Office
Jan 03:	FORSCOM requests Department of Army letter of support
28 Jan 03:	Final HSRRB approval
31 Jan 03:	MRMC Commander provides DA letter of support
28 Feb 03:	FORSCOM identifies initial units (primarily regular Active Duty, Fort Hood); III Corps requests FORSCOM tasking order
Mar 03:	Start-up funds received
Mar 03:	Assistant Secretary of Defense provides letter of support FORSCOM tasks III Corps Scheduled by III Corps to begin data collection 27 Mar
22 Mar 03:	4th Infantry Division receives flight orders/opts out of study
3–9 Apr 03:	301 "deploying" Soldiers (1st Cavalry Division) assessed (Time 1)
14–18 Apr 03:	149 "non-deploying" Soldiers assessed
14 Apr 03:	Deployment orders of 1CD called into question (eventually cancelled)
Aug 03:	FORSCOM identifies two Active Duty Stryker brigades appropriate to study 3/2 SBCT to serve as deploying group; 1/25 SBCT to serve as non-deploying group Intent to deploy 1st Cavalry Division announced
Nov 04:	3/2 SBCT deploys
22 Sep- 9Oct03:	450 3/2 SBCT and 387 1/25 SBCT Soldiers assessed (Time 1)
Dec 04:	2nd baseline (Time 1.5) conducted on 1st Cavalry Soldiers to provide assessment more proximal to actual deployment
Feb 04:	1st Cavalry deploys
May 04:	Intent to deploy 1/25 SBCT announced; Time 2 assessment (post-garrison duty) conducted FORSCOM identifies 278th ARNG unit as appropriate National Guard study component
July 04:	Soldiers from 1/25 SBCT not available in May 04 assessed 278th ARNG assessed (Time 1)
Sep 05:	1/25 SBCT deploys
Nov 05:	3/2 SBCT returns
Dec 05:	278th ARNG deploys (1 month earlier than originally anticipated) To provide an Active Duty comparison that was deployed contemporaneously with ARNG unit, plans are made to assess 1/25 SBCT upon their return.
Jan 05:	Post-deployment assessment conducted on 3/2 SBCT
Mar 05:	1st Cavalry returns
May 05:	Post-deployment assessment conducted on 1st Cavalry and other III Corps units
Aug 05:	Plans made to assess 3/2 SBCT (Time 3) in Sept 05 Katrina displaces New Orleans study team, preventing travel; Sept assessment rescheduled to Dec 05
Oct 05:	Major study equipment retrieved from New Orleans
Dec 05:	Time 3 (follow-up post-deployment assessment conducted on 3/2 SBCT)
Jan 06:	Time 3(initial post-deployment survey) conducted on 1/25 SBCT (unit formerly a non-deployed comparison during the Time 1 to Time 2 interval)
April 06:	Time 2 (post-deployment) assessment of ARNG unit
May 06:	Time 2 (post-deployment) assessment of ARNG unit
Jun 06:	Time 2 (post-deployment) assessment of ARNG unit
Sep 06:	Time 2 (post-deployment) assessment of ARNG unit
Aug 06:	Time 3 assessment completed on 1st Cavalry
Feb 07:	PI moves research laboratory to Boston

July-Nov 07: Time 2 assessment completed by mail on GA ANG non-deployed unit
Time 3 assessments completed by mail on ARNG units
Time 3 assessments completed by mail on 1st Cav soldiers who were not available for in person assessment in Aug 06.

The current timeline now includes Time 3 administrative data collection, data analysis and preparation of final reports extending through January 2009. Therefore the final, approved SOW is as follows:

STUDY TIMETABLE –MODIFIED STATEMENT OF WORK

YEAR 1		
Task 1	Proposal phase and Week 1	Orient project staff to project tasks, training)
Task 2	Months 1-3	Set-up and baseline (Time 1) assessment of Ft. Hood participants
Task 3	Months 4-10	Establish data base; as relevant to Task 2 participants, collection of electronic medical/health care record system databases through data requests, transfer of test data to format readable by statistical software; data entry of data generated by Task 2
Task 4	Months 6-12	Re-assessment of Ft. Hood participants to correspond more closely to their rescheduled deployment date; baseline (Time 1) assessment of Ft. Lewis participants (3/2 Stryker Brigade Combat Team (SBCT); 1/25 Stryker Brigade Combat Team (SBCT);
YEAR 2		
Task 1	Months 13-18	As relevant to Task 4 participants, collection of electronic medical/health care record system databases through data requests, transfer of test data to format readable by statistical software; data entry of data generated by Task 4
Task 2	Months 13-24	Collection of Time 2 data relevant to Ft. Lewis participants
Task 3	Months 13-24	Collection of Time 1 data; deploying National Guard cohort
YEAR 3		
Task 1	Months 25-26	Collection of postdeployment data; Fort Hood participants
Task 2	Months 27-36	Collection of electronic medical/health care record system databases through data requests, transfer of test data to format readable by statistical software; data entry of data generated; data analysis and preparation of reports on all participants included in protocol to date.
Task 3	Months 34-36	Collection of Time 3 data on Fort Lewis participants
YEAR 4		
Task 1	Month 43	Collection of Time 3 (2nd post-deployment) data on Fort Hood participants
Task 2	Months 39-44	Collection of post-deployment data on National Guard participants
Task 3	Months 36-43	Scientific review and publication of primary T1/T2 Active Duty findings
YEAR 5		
Task 1	Months 52-54	Collection of Time 3 data on National Guard participants and final mail data collection on all other participants not available for in person Time 3 assessment
Task 2	Months 54-60	Collection of electronic medical/health care record system databases through data requests, transfer of test data to format readable by statistical software; data entry of data generated relevant to Year 4, Task 3 & Year5, Task 1 participants.
YEAR 6	Months 61-72	Data analysis and preparation of final reports.

Progress to date

Progress to date includes accomplishment of all tasks through Year 5, with the exception of integration of medical record data from ARNG units, which must be requested separately. In addition to the elements explicitly listed within the SOW, we continue to use our administrative infrastructure, have kept in place and renewed, as appropriate, all necessary administrative approvals, and continue to be in contact with members of our Scientific Advisory Council. In addition to publications from previous years (*Military Medicine, 2006; Journal of the American Medical Association, 2006)*, in Year 5, we published a manuscript describing rates of baseline posttraumatic stress disorder (PTSD) and the relationship of PTSD symptoms to early life events and unit cohesion is currently in the *Journal of Traumatic Stress*, Vol. X, 2007 (see appendix). We also have had two manuscripts accepted for publication, which are both currently in press. The first describes the relationship of postdeployment PTSD symptoms to health-related functioning among active duty soldiers who deployed to Iraq. It is in press in the *Journal of Rehabilitation Research* (see appendix). The second examines the psychometric qualities of the *Deployment Risk and Resilience Inventory,* our primary measure of stress exposures, within deployed members of the cohort. This manuscript is currently in press in the journal, *Assessment*.

All primary data have been entered and subjected to intensive data quality checks. Data management has required extensive effort because of the anomalies regarding participant classification as "deployed" or "non-deployed" and the addition of a second baseline for the 1st Cavalry unit. However, a comprehensive and synthesized data base had been established. Primary outcomes for Time 1 to Time 2 have been conducted for the Active Duty component. We have recently completed analyses relevant to secondary objectives (PTSD outcomes) for Time 1 to Time 2 Active Duty and National Guard participants. A manuscript describing these outcomes was submitted to a scientific journal in January 2007 and is currently under scientific review.

Time 1 enrollment totaled 1595 participants. Time 2 assessments have been conducted on all participating units and include a total of 1173 participants. Longitudinal retention from Time 1 to Time 2 for Active Duty Soldiers has been approximately 76.7%. Among those who were not retained for Time 2 assessment, the primary reasons for loss to follow-up have been changes in military unit assignments (14%) and separation from service (46.1%). Longitudinal retention of Army National Guard Soldiers has been lower (61%) and reflects re-organization within the 278th and, more often, separation from the National Guard.

Time 3 (1-year follow-up) in-person assessments were conducted on a much smaller subgroup of active duty soldiers (n= 186) who remained in the military with their originating units. One-year follow-up mail surveys were completed by an additional 85 soldiers (active duty and National Guard) who we were not able to follow with in person surveys. In addition, we have completed the initial post-deployment assessment of a brigade that had been assessed previously before and after a period of garrison duty but subsequently deployed (n = 108 in person; n = 18 mail survey). We are currently in the process of analyzing these data for publication.

Findings to date

1. Primary outcomes: Neuropsychological functioning

Findings from multi-level analyses that take into account battalion-level unit membership and demographic covariates indicate that deployment was associated with disadvantages to memory functioning (as measured by a non-computerized word list learning task, WMSIII Verbal Paired Associates I sum and a visual reproduction task, WMS Visual Reproductions delay and savings ratio) and attention (as measured by number of non-response errors on a computerized simple continuous performance task, NES3 CPT), but advantages to reaction time efficiency (ANAM Simple Reaction Time). All other tasks of cognitive efficiency (ANAM) were unaffected. Additionally, deployment was associated with adverse changes in emotional functioning, including symptoms associated with posttraumatic stress disorder (PTSD) and state affect, including POMS Confusion and Tension scores. In contrast, deployment was not associated with changes in measures of state (POMS) depression, vigor, anger, or fatigue, or measures of functional health (SFv12 and MOS Cognitive) including self-perceptions of cognitive, emotional, and physical functional impact.

These findings have been published in the *Journal of the American Medical Association* (see February 2007 report).

2. Secondary outcomes: PTSD

a. Stressful life events, unit cohesion, and PTSD prior to deployment

We examined relationships among stressful life events, perceived unit cohesion, and PTSD symptom severity at Time 1 across the entire NDHS cohort. We found that a sizable subset of military personnel (10%) reported significant pre-deployment, stress-related symptoms, as measured by the PCL, a 17-item DSM-based self-report survey, and using the criteria established by Hoge et al. (2004). Regression analyses revealed that life experiences (beta = 1.20, p <.001) and unit cohesion (beta = -0.35, p < .001) independently predicted PTSD symptoms at baseline, together predicting 22% of the variance, even after taking into account demographics and duty status.

A scientific manuscript describing these findings was published in the *Journal of Traumatic Stress* (see attachment).

b. PTSD outcomes as a function of deployment

We analyzed the PTSD outcome data of 779 participants who deployed to Iraq between Time 1 and Time 2, comparing them with 315 soldiers similar in military characteristics who did not deploy between Time 1 and Time 2. PTSD symptom severity was measured with the PTSD Checklist. We also used the PTSD Checklist to estimate screening diagnoses. Using the Deployment Risk and Resilience Inventory, we additionally examined the influence of lifetime, war-zone, homefront, and post-deployment stress exposures on PTSD outcome. We found that deployment was associated with greater PTSD severity (B=3.61;P<0.001) and almost a threefold higher risk of developing PTSD (OR=2.97, CI = 2.56,3.46). PTSD cases among deployed soldiers increased from 7.6% before deployment to 12.1% following deployment. Although PTSD did not differ significantly at post-deployment between National Guard and active duty soldiers, PTSD increased more among National Guard soldiers who reported fewer PTSD symptoms prior to deployment than active duty soldiers. War-zone events, homefront concerns, and post-deployment life events were associated with PTSD symptoms among all deployed soldiers, but post-deployment life events were more strongly associated with PTSD symptoms in National Guard soldiers. These analyses provide stronger evidence than previously possible that war-zone deployment is associated with increased risk of PTSD. Findings also highlight the impact of homefront and post-deployment life events in addition to war-zone stress exposures, and emphasize the importance of continued attention to the concerns of reservists.

A manuscript describing these findings was submitted in January 2008 and is currently under scientific review.

c. The relationship of PTSD to health related functioning

Preliminary analyses of available NDHS data conducted during the previous reporting period suggested that self-reported day-do-day functioning related to *cognitive and somatic health problems* declined among both deployed and non-deployed active duty participants, but that deployment status did not interact significantly with time. As shown in the following table, there were no significant changes from Time 1 to Time 2 in self-reported *mental health-related functioning* among either deployed or non-deployed participants. These findings highlight the significance of neuropsychological and health-related changes on day-to-day functioning, but raised the question that factors other than deployment status alone might influence such changes.

Paired t-tests (Time 1 v. 2) within each deployment group with functional impact scores as outcome variables

	Deployed (n = 674)		Non-deployed (n = 315)	
	Time 1	Time 2	Time 1	Time 2
Physical Component, SF12v	51.85 (7.00)	50.61 (7.46)***	51.82 (7.39)	50.49 (8.53)**
Mental Component, SF12v	49.62 (10.78)	49.77 (10.57)	48.90 (11.12)	48.26 (11.77)
Cognitive functioning	78.02 (20.13)	73.51 (21.10)***	77.47 (19.77)	74.70 (22.26)**

Mean (sd); **p< 0.01; ***p <0.001, paired t-tests (Time 1 v. 2) within each deployment group

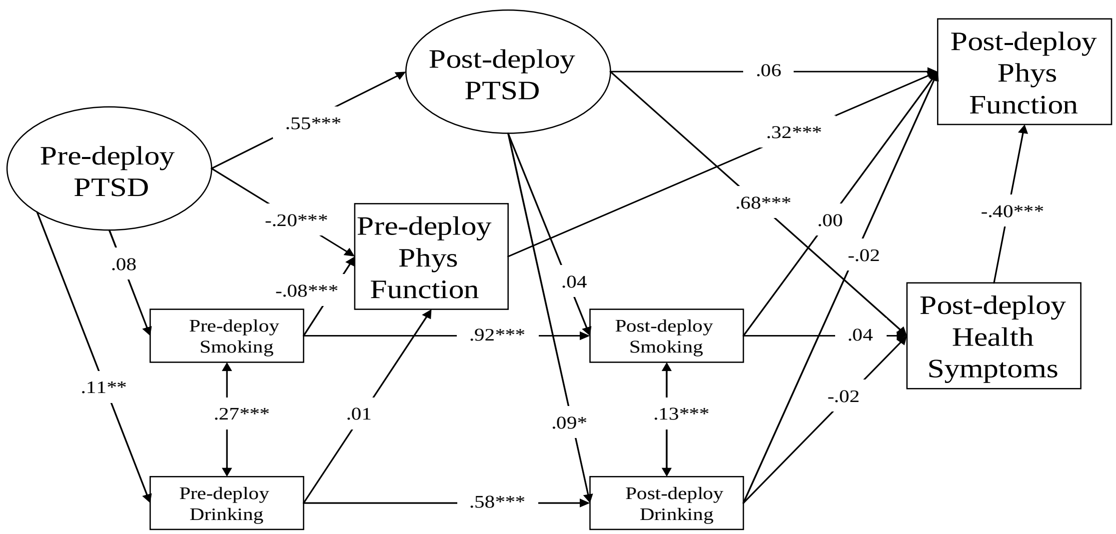
To examine a specific factor within the deployment context that might account for decline in health-related functioning among deployed soldiers, we followed our preliminary analyses with a structural equation model testing the relationship between post-deployment PTSD symptoms and longitudinal change in health-related outcomes, physical symptoms, and health-behaviors. The analyses were conducted on 800 soldiers who deployed to Iraq. As shown in the following table and figure, structural equation modeling revealed that post-deployment PTSD severity was associated with decline in somatic health functioning through post-deployment health symptoms as an intermediary variable. These relationships were independent of health risk behaviors, which had little association with somatic symptoms or PTSD. Findings highlight the functional impact of PTSD, which extends beyond psychological symptoms to health-related day-to-day functioning.

SEM model standardized effects of post-deployment model predictors on post-deployment physical health functioning while controlling for pre-deployment physical health functioning.

Variable	Direct Effects	Indirect Effects	Total Effects
Post-deployment smoking	.00	-.02	-.02
Post-deployment drinking	-.02	.01	-.01
Post-deployment PTSD	.06	-.28***	-.22***
Post-deployment health symptoms	-.40***		-.40***

Note. PTSD = posttraumatic stress disorder. ****p* < .001.

Visual representation of result of the structural equation model examining relationships among post-deployment PTSD, longitudinal change in health behaviors (i.e., smoking, alcohol consumption), post-deployment health symptoms, and longitudinal change in health related functioning.



A manuscript describing these analyses is currently in press in the *Journal of Rehabilitation Research and Development* and can be found attached in the appendix to this report.

The next steps in the analyses will be: (1) examination of the longitudinal associations among neuropsychological functioning, traumatic brain injury, and PTSD; (2) examination of the duty status, comparing the deployed Army National Guard Unit outcomes to those of an Active Duty participants matched as closely as possible for demographics, MOS, and deployment stress exposures; (3) examination of the association between PTSD development and standardized test taking ability among deployed active duty soldiers; and (4) examination of the longitudinal stability of findings at 1-year follow-up.

KEY RESEARCH ACCOMPLISHMENTS

Publications

Vasterling, J., J., Schumm, J., Proctor, S. P., Gentry, E., King, D., & King, L. (in press). PTSD and health functioning in a non-treatment seeking sample of Iraq War veterans: A prospective analysis. *Journal of Rehabilitation Research and Development.*

Vasterling, J. J., & MacDonald, H. (in press). Neuropsychological functioning and posttraumatic stress disorder: Implications for war-zone veterans. *Harvard Health Policy Review.*

Brailey, K., Vasterling, J. J., Proctor, S. P., Constans, J. I., & Friedman, M. J. (2007). PTSD symptoms, life events, and unit cohesion in U.S. Soldiers: Baseline findings from the Neurocognition Deployment Health Study. *Journal of Traumatic Stress, 20,* 495-504.

Vasterling, J. J., Proctor, S. P., Amoroso, P., Kane, R., Heeren, T., & White, R. F. (2006). Deployment to the Iraq War and neuropsychological sequelae: Letter in reply. *Journal of the American Medical Association, 296,* 2679-2680.

Vasterling, J.J., Proctor, S. P., Amoroso, P., Kane, R., Heeren, T., & White, R.F. (2006). Neuropsychological Outcomes of Army Personnel Following Deployment to the Iraq War: A Prospective Examination. *Journal of the American Medical Association, 296,* 519-529.

Vasterling, J.J., Proctor, S. P., Amoroso, P., Kane, R., Gackstetter, G., Ryan, M.A.K., & Friedman, M.J. (2006). The Neurocognition Deployment Health Study: A prospective cohort study of Army soldiers. *Military Medicine, 171*, 253-260.

Presentations

Vasterling, J. J. (December, 2007). *Initial Findings from the NDHS: Neuropsychological and PTSD Outcomes*. Presentation to the Department of Defense Health Affairs, Deployment Health Support Directorate. Falls Church, VA.

Vasterling, J. J. (November, 2007). *Initial Findings from the NDHS: Neuropsychological and PTSD Outcomes*. International Society for Traumatic Stress Studies Pre-Meeting Institute presentation. Baltimore, MD.

Vasterling, J. J. (November, 2007). *TBI, PTSD, and Neuropsychological Outcomes in Iraq-Deployed US Army Soldiers: (Very) Preliminary Findings.* International Society for Traumatic Stress Studies Late Breaking Panel presentation. Baltimore, MD.

Vogt, D.S., Proctor, S. P., & Vasterling, J. J. (June, 2007). Psychometric properties of the DRRI among Iraq War veterans. Paper presented at the 10th European Conference on Traumatic Stress. Opatija, Croatia.

Rutkowski, L., Vasterling, J.V., & Proctor, S.P. (2007). *PTSD and standardized test performance: An example of IRT with covariates.* Paper presented at the 2007 annual American Educational Research Association Annual meeting. Chicago, IL.

Proctor, S. P., & Vasterling, J. J. (November, 2006). *Comparison of active duty and national guard soldiers on pre-deployment factors: Findings from the NDHS.* Paper presented at the 22nd Annual Meeting for the International Society for Traumatic Stress, Los Angeles, CA.

Vasterling, J. J. & Proctor, S. P. (November, 2006). *Prospective analysis of memory functioning and PTSD in Army soldiers: Findings from the NDHS.* Paper presented at the 22nd Annual Meeting for the International Society for Traumatic Stress, Los Angeles, CA.

Vasterling, J. J. (August, 2006). *The Neuropsychology of PTSD: Longitudinal Findings from the Neurocognition Deployment Health Study (NDHS).* Division 40 Invited Presentation to the American Psychological Association Convention 2006, New Orleans, LA.

Rutkowski, L., Proctor, S.P., & Vasterling, J.J. (November, 2006). *Explanatory item response theory in trauma research*. Paper presented at the Annual Conference on Innovations in Trauma Research Methods meeting. Hollywood, CA.

Vasterling, J. J. (June, 2005). *Examining the Neuropsychological Outcomes of Iraq Deployment: A Model of Effective DoD/VA Research Collaboration.* Invited presentation at the National Mental Illness Research, Education, and Clinical Center 2005 Conference, New Orleans, LA.

Proctor, S. P., & Vasterling, J. J. (May, 2004). *Update: From the Gulf War to Operation Iraqi Freedom*. Invited presentation for the USARIEM Environmental Medicine Course 2004, Natick, MA.

Vasterling, J. J. (July, 2004). *Prospective Assessment of Psychological and Neuropsychological Functioning in Iraq-deployed Army Troops: A Preliminary Cross-sectional Report.* Invited paper presentation at the VISN 16 MIRECC/National Center for PTSD Summit Meeting, Resilience and Treating Early PTSD, New Orleans, LA.

Vasterling, J.J., Proctor, S. P., & Kane, R. (October, 2003). *Prospective Assessment of Gulf-deploying and Gulf-nondeploying troops.* Paper presented at the 19th Annual Meeting for the International Society for Traumatic Stress, Chicago, IL.

Vasterling, J. J. & Proctor, S. P. **(**May, 2003). *Prospective Assessment of Iraq-deploying and Non-deploying Troops: An Interdepartmental Effort.* Invited presentation to the Research Subcommittee of VA/DoD Deployment Health Work Group, Washington, D.C.

Vasterling, J. J. & Proctor, S. P. (June, 2003). *Prospective Assessment of Iraq-deployed Troops.* Invited presentation to the Research Advisory Council on Gulf War Veterans Illnesses, Washington, D.C.

REPORTABLE OUTCOMES: THIS REPORTING PERIOD

- please see attached *Journal of Traumatic Stress* publication
- please see attached manuscript in press, *Journal of Rehabilitation Research*
- manuscript in press, *Assessment*
- please see attached manuscript in press, *Harvard Health Policy Review*
- 5 national/international scientific presentations, as listed above
- a 1 year DoD CDMRP Concept Award was funded to perform secondary data analysis on the study cohort to examine questions regarding the relationship of mild traumatic brain injury and neuropsychological outcomes
- a 5.5 year VA multi-site cooperative study (CSP#566, "Neuropsychological and Mental Health Outcomes of Operation Iraqi Freedom (OIF): A Longitudinal Cohort Study") to complete a subsequent wave of data collection on the study cohort was approved and funded
- information from the application of the ANAM in this study has been used to inform modification and quality assurance assessment of the ANAM
- information from the administration of the Deployment Risk and Resilience Inventory has been used as the basis of a VA-funded grant to examine its psychometric characteristics and refine item content to optimize use with OIF/OEF populations
- information about the process of the project was used by the VA International Scientific Forum to help inform items of relevance to the worldwide scientific agenda regarding veterans health issues

CONCLUSIONS

Process Conclusions

This study has established an effective model of inter-departmental collaboration between VA and DoD. This is a critical accomplishment relevant especially to longitudinal research addressing outcomes throughout both military and post-military life periods.

In addition, the work accomplished has provided a model of how neurobehavioral assessments could potentially be incorporated into more regular surveillance with the military. With memory and other cognitive complaints factoring high among war-zone returnees and being of high relevance to occupational functioning and cognitive readiness, the establishment of neurobehavioral surveillance methodology is significant to force health protection efforts. The methods used in this study are non-invasive and could potentially be implemented in a cost-effective manner on a broader scale. A manuscript regarding the utility of neuropsychological surveillance in military and military veteran populations is currently in press in the *Harvard Health Policy Review*.

Scientific Conclusions

Findings to date suggest that there are objective changes in neuropsychological functioning associated with deployment. While at least one is at face value positive (efficiency in simple reaction time), others are negative (less proficient attentional and memory performances, increased emotional symptoms). Taken together, findings raise the question of a biological stress response, involving neurotransmitter/hormonal systems relevant to the neurobehavioral findings listed above. The design elements of a baseline assessment and of a non-deploying comparison sample well-matched to the deploying sample on key demographic and military characteristics suggest that these findings cannot be attributed solely to pre-existing conditions or simply to the passage of time.

Analysis of PTSD outcomes yielded several major conclusions. First, significant numbers of military personnel reported significant life events and elevated stress symptoms at baseline. However, these symptoms are buffered by unit cohesion, a potentially modifiable risk factor. Second, deployment to Iraq is associated with increased risk of new onset PTSD, particularly among soldiers with greater deployment, homefront, and post-deployment stress exposures and among those activated from National Guard duty status. These findings hold implications for preventive healthcare. Namely, if soldiers can be prepared for the types of stressor they are most likely to encounter, they may be better able to cope with these events. Our findings also suggest the continued need to attend to re-integration its associated stressors and to the special concerns of National Guard members and other reservists. Finally, post-deployment PTSD symptoms are associated with longitudinal declines in health-related functioning, which appear secondary to post-deployment health symptoms. This finding highlights the associations between stress and somatic health, suggesting that they may manifest much earlier than previously thought.

The ongoing work will also allow examination of whether these findings are stable over time, if longer-term outcomes can be predicted by early neurobehavioral markers, whether duty status (regular Active Duty versus Guard/Reserve) influences outcomes, and the impact of adverse outcomes on occupational functioning and service utilization with DoD and VA medical care facilities. Finally, our screening for head injury over the deployment period will allow exploration of associations between neurocognitive functioning, traumatic brain injury, and emotional functioning.

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Appendix

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PTSD Symptoms, Life Events, and Unit Cohesion in U.S. Soldiers: Baseline Findings From the Neurocognition Deployment Health Study

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Relationships among a modifiable situational factor (unit cohesion), prior stressful life events, and posttraumatic stress disorder (PTSD) symptoms were assessed in 1,579 U.S. Army soldiers with no history of contemporary war zone deployment. It was predicted that unit cohesion would attenuate the dose-response relationship between past stressor exposures and PTSD symptoms at relatively moderate levels of exposure. Consistent with this hypothesis, regression analysis revealed that life experiences and unit cohesion strongly and independently predicted PTSD symptoms, and that unit cohesion attenuated the impact of life experiences on PTSD. Some military personnel reported significant predeployment, stress-related symptoms. These symptoms may serve as vulnerabilities that could potentially be activated by subsequent war-zone deployment. Higher predeployment unit cohesion levels appear to ameliorate such symptoms, potentially lessening future vulnerability.

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High rates of posttraumatic stress disorder (PTSD) have been documented among war-zone veterans (Duke & Vasterling, 2005), with some evidence suggesting that a dose-response relationship exists between war-zone stressor severity and PTSD symptom levels (see Dohrenwend et al., 2006, for a recent example). A variety of risk and resilience factors have been tentatively identified as modifying this relationship (see King, Vogt, & King, 2004; Maguen, Suvak, & Litz, 2006, for summaries). With large numbers of military personnel now deployed to combat situations, it is essential for health planning efforts to take into consideration the broader scope of factors potentially influencing mental health functioning in military personnel. In particular, because emotional functioning has rarely been assessed prospectively, prior to deployment, the impact of prewar-zone risk and resilience factors on postwar-zone mental health may not be fully appreciated. Understanding how individuals' predeployment personal histories and situational factors influence emotional functioning, including preexisting PTSD symptoms, prior to war-zone deployment may be critical to development of both predeployment preventive and postdeployment treatment interventions.

The primary purpose of this report is to describe risk and resilience factors potentially impacting troops prior to warzone deployment. Specifically, demographic, stressor exposure variables, and situational factors were measured in a large cohort of Army soldiers who had not yet been deployed to either Operation Iraqi Freedom (OIF) or Operation Enduring Freedom (OEF). As a situational factor, we focused on unit cohesion, a contextual military variable.

We chose to examine unit cohesion for several reasons. First, unit cohesion is potentially modifiable and therefore a candidate for integration into preventive mental health care policy. Second, unit cohesion is an intuitive construct historically recognized within military culture as having positive impact (Shay, 1994; von Clausewitz, 1832/1989). Finally, theoretical models of unit cohesion suggest that high levels of unit cohesion should constitute a major resilience source for military-related stressors, including those associated with combat (e.g., Bliese, 2006; Griffith & Vaitkus, 1999).

Empirical support for this assertion is generally positive, with numerous studies demonstrating that high levels of unit cohesion impart the expected resilience to cope with typical military-related stressors (see the meta-analysis by Oliver et al., 1999, for a review), and several studies demonstrating the resilience effect for combat-related stressors (e.g., McTeague, McNally, & Litz, 2004; Solomon & Mikulincer, 1990; Solomon, Mikulincer, & Hobfoll, 1986). In contrast, Fontana, Rosenheck, and Horvath (1997) found that whereas low to moderate unit cohesion was related to lower reported rates of PTSD symptoms, very high levels of unit cohesion were associated with higher than expected levels of PTSD symptoms among Vietnam combat veterans.

Consistent with the findings of Fontana et al. (1997), Suvak, Vogt, Suvarese, King, and King (2002) found a curvilinear interaction between various aspects of coping and life adjustment, with stress exposure levels moderating the interaction. More specifically, they demonstrated that the positive effect of problem-focused coping on quality of life increased as exposures mounted to moderate levels, but that the effect reversed (i.e., increases in problem-focused coping led to steadily decreasing levels of quality of life) when exposures surpassed moderate levels. Suvak et al. suggested that relatively high levels of problem-focused coping have increasing benefits as stressor levels mount to moderate levels due to the perception that the challenge presented by the mounting stressors is successfully being met. However, at the point at which stressors become overwhelming (e.g., during combat when a unit is incurring casualties that it cannot effectively curtail or is being overrun), the uncontrollability of the situation renders high levels of problem-focused coping counterproductive. This curvilinear interaction is hypothesized to be consistent with goodness of fit theories regarding effective coping (see Park, Folkman, & Bostrom, 2001, for recent support and review). By such theories, some coping mechanisms (e.g., problem-focused coping) are inappropriate in situations that have become uncontrollable.

Most formulations regarding the protective effects of unit cohesion on stress emphasize the formation of trust by an individual in both his or her compatriots and supervisors, a dichotomy that Griffith and Vaitkus (1999) refer to as horizontal/peer versus vertical/leader bonding. This trust is considered by military leaders to be the emotional foundation that prevents the breakdown of problem-focused communication and problem solving under high levels of threat. As stress levels mount from low to medium levels, high levels of unit cohesion could help to engender confidence in members of a unit under attack, helping them to engage in problem-focused coping that proves to be effective. However, as stress levels become overwhelming and effective problem solving ineffectual, high levels of unit cohesion may be later seen as an illusion that has been betrayed, a formulation consistent with Fontana et al.'s (1997) suggestion that high levels of unit cohesion potentially lead to a consensual appraisal of a negative outcome as a catastrophe by surviving unit members.

Predictions were based on the assumption that, although military personnel will have experienced a range of prior life stressors, their immediate context (even if preparing for a deployment) would be characterized by the absence of overwhelming levels of stress. Specifically, we predicted that, whereas both stressful life events and unit cohesion would be independently associated with PTSD symptom levels prior to deployment, unit cohesion would also moderate the relationship between life events and PTSD. Given the restricted range of current stress levels in the nonwarzone environment for most participants, we did not expect this moderation effect to exhibit any curvilinear effects.

METHOD

Participants

Participants were Army soldiers assessed as part of the Neurocognition Deployment Health Study (NDHS; Vasterling et al., 2006; Vasterling, Proctor, Amoroso, Kane, Heeren, & White, 2006). Participants were sampled at the battalion-level military unit, with military units selected to reflect a mix of combat arms, combat support, and combat service support functions. Active duty units, comprising the majority of units, originated from Fort Hood, Texas, and Fort Lewis, Washington. National Guard units originated from Tennessee, Georgia, and Wisconsin. Assessment data reported here were gathered from April 2003 to July 2004. At the time, no unit had been deployed overseas as part of either OIF or OEF. Of 1,699 potential participants invited to participate, 1,595 agreed, reflecting a participation rate of 94%. Twelve participants were eliminated from data analyses for failure to complete major portions of the assessment, and four were removed due to missing information critical to PTSD diagnostic determination, leaving a final sample of 1,579. Of this group, 10% were women, 38% self-reported being a member of an ethnic minority, and 51% single. The sample averaged 26.0 years in age ($SD = 6.1$) and completed 12.6 years of formal education ($SD = 1.4$). Rank groupings included 71% categorized as junior enlisted (E1–E4), 25% as noncommissioned officers ($\geq$E5), and 4% as officers. Prevalent military occupations included infantry/gun crew (34%), electrical/mechanical repair (20%), communication/intelligence (20%), and service supply (10%). Eighty-six percent were regular active duty and 14% were activated reservists; 10% had served in a previous overseas operational deployment during their entire career, but only 2% had experienced an overseas operational deployment since September, 2001.

Measures

The PTSD Checklist (PCL), a widely-used 17-item self-report scale designed to measure distress associated with each PTSD symptom (King, Leskin, King, & Weathers, 1998; Weathers, Litz, Herman, Huska, & Keane, 1993), was used to derive *DSM-IV* (*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*; American Psychiatric Association, 1994) PTSD diagnoses. Initial validation efforts demonstrated good internal consistency for both the overall scale ($\alpha = .95$) and subscales measuring PTSD Criteria B, C, and D (αs ranging from .89 to .92). Cross-validation efforts comparing PCL diagnoses of PTSD with diagnoses derived from clinician-administered structured interviews have demonstrated acceptable accuracy as measured by kappas of .64 for a sample of Vietnam veterans (Weathers et al., 1993) and .83 in a sample of motor vehicle accident and assault victims (Blanchard, Jones-Alexander, Buckley, & Forneris, 1996).

In this study, participants were asked to link their PCL responses to a stressful life event from their past. Subscales of a modified version of the Deployment Risk and Resilience Inventory (DRRI; King, King, Vogt, Knight, & Samper, 2006) documented stressful life events (17 items reflecting exposure to stressors such as physical and sexual assault, serious accident and physical injury, etc.) and military unit cohesion (12 items reflecting unit support and satisfaction with leadership such as "members of my unit understand me," "my unit is like family to me," "I am impressed by the quality of leadership in my unit," "the military appreciates my service"). Development of all DRRI scales reflect a rational test development process in which constructs under scrutiny were defined by expert consensus. Final test items, including life events and unit cohesion items, were selected on the basis of cross-validation studies conducted with two samples of military populations. Internal consistency scores for both scales were as expected (life events $\alpha = .75$; unit cohesion $\alpha = .94$), with the relatively moderate life events alpha reflecting predicted heterogeneity in life stressors (see King et al., 2006, for further discussion.)

Procedures

Participants completed demographic and self-report measures in small groups at military installations (Vasterling, Proctor, Amoroso, Kane, Gackstetter, Ryan, et al., 2006). Outliers greater than three standard deviations from each scale mean were recoded to the most extreme range value within three standard deviations of the mean. Missing values for PCL, unit cohesion, and life events scale items were extremely infrequent (missing data percentages were .2, .4, and .2 for each scale, respectively). For the PCL and unit cohesion subscales, missing data were imputed ideographically from all items present for a specific subscale. Missing life events items were omitted due to unreliability in estimating *yes/no* responses.

RESULTS

The mean PCL score for study participants was 29.41 ($SD = 12.77$). To meet minimal *DSM*-related criteria, a PTSD diagnosis was assigned to cases in which moderate or higher responses (i.e., ≥ 3 on a 5-point Likert scale item) were provided for at least one intrusion symptom (Criterion B), three avoidance/numbing symptoms (Criterion C), and two hyperarousal symptoms (Criterion D); following Hoge et al. (2004), a minimum PCL score of 50 was required in addition to the *DSM*-prescribed pattern. Using this decision rule, the percentage of study participants meeting full PCL-derived PTSD criteria was 10%.

Factors Predicting Posttraumatic Stress Disorder

A hierarchical regression equation adjusted for demographic variables examined the associations of stressor exposure and unit cohesion with PTSD symptoms. The dependent variable was total PCL score, with higher values indicating greater levels of PTSD symptoms. Independent variables were centered and entered in two steps. Step 1 contained the independent variable of interest (life events and unit cohesion scores). In addition, to examine the associations of life events and unit cohesion independently of potential confounding variables, Step 1 contained military variables and demographic variables commonly identified as covarying with PTSD: gender, age, rank (junior enlisted vs. noncommissioned officer/officer), marital status (married vs. not married), education (in years), self-reported ethnicity (White vs. minority), duty status (active duty vs. reservist), and prior career deployment status (yes vs. no). Step 2 contained a product term for life events and unit cohesion (Life Events $\times$ Unit Cohesion) to examine possible linear moderation effects. Following statistical recommendations of Aiken and West (1991) and Suvak et al. (2002), two additional terms were included at Step 3 to test for potential curvilinear or quadratic effects. The first term reflects the hypothesized curvilinear relationship of the life event variable with the dependent variable; the term is constructed by squaring the life events scale (life events^2). The second term is the quadratic term, which specifically estimates potential curvilinear interaction effects; this term is derived by taking the product of the squared life events scale and the unit cohesion scale (life events^2 × unit cohesion).

Analysis of variance (ANOVA) tests were significant for the initial regression model at Step 1 and the model after Step 2 (see Table 1). At Step 1, younger age, minority status, and higher levels of life stress were associated with greater PCL scores, whereas higher unit cohesion was associated with lower PCL scores. Secondary analyses indicate that life events and unit cohesion effects, even when controlling for covariance with demographic factors, predominated at Step 1, together accounting for 22% of the total variance in PCL scores. The linear moderator effect at Step 2 was significant, though small ($\Delta R^2 = .004$); such small moderator effect sizes are to be expected, given constraints on main effects typically found in social science experiments (Cohen, Cohen, West, & Aiken, 2003). The overall fit of the model did not significantly improve with the inclusion of Step 3 variables, $F < 1$; $\Delta R^2 = .001$; t tests were not significant for either the curvilinear aspect of life events, $\beta = .03$, *ns*, or importantly, for the curvilinear interaction term, $\beta = .01$, *ns*. These null results suggest that the moderator effect is linear in nature and that terms reflecting a curvilinear effect should not be included in the final model. All variables significant at Step 1 remained significant in the final model.

The significant moderator effect can be interpreted in two complimentary ways. Simple slope tests of the moderator (Aiken & West, 1991) indicate (a) that associations between life events and PCL scores weakened as unit cohesion increased, and (b) that associations between unit cohesion and PCL scores strengthened (e.g., the magnitude of reductions in PCL scores associated with increasing levels of unit cohesion) as the incidence of stressful life events increased. The latter presentation is consistent with models that predict increasing effectiveness for unit cohesion in mitigating PTSD symptoms when levels of stressors are at low to medium levels. Step 2 effects therefore suggest that unit cohesion is associated with PTSD symptoms both directly (increasing unit cohesion levels are independently associated with decreasing PCL scores) and indirectly (increasing unit cohesion levels are associated with decreased influence of life events on PCL scores).

Table 1. Hierarchical Regression Analysis for Centered Demographic, Life Events, Unit Cohesion, and Moderator Variables Predicting Posttraumatic Stress Disorder ($N = 1{,}579$)

Variable	B	$SE\ B$	β
Step 1			
Gender	1.35	0.95	.03
Age	−0.16	0.06	−.08**
Rank	−0.96	0.77	−.03
Marital status	−0.39	0.60	−.02
Education	−0.28	0.21	−.03
Ethnicity	−2.40	0.60	−.09***
Prior deployment	−0.79	1.03	−.02
Reserve status	−0.50	0.88	−.01
Life events score	1.20	0.08	.32***
Unit cohesion score	−0.37	0.03	−.32***
Step 2			
Gender	1.30	0.95	.03
Age	−0.16	0.06	−.08*
Rank	−1.03	0.77	−.04
Marital status	−0.40	0.60	−.02
Education	−0.26	0.21	−.03
Ethnicity	−2.42	0.60	−.09***
Prior deployment	−0.74	1.03	−.02
Reserve status	−0.53	0.88	−.01
Life events score	1.18	0.08	.32***
Unit cohesion score	−0.37	0.03	−.32***
Life Events × Unit Cohesion term	−0.02	0.01	−.06**

Note. For Step 1, $R^2 = .26$, $F(10, 1568) = 55.60$, $p < .001$; for Step 2, $\Delta R^2 = .004$, $\Delta F(1, 1567) = 8.55$, $p < .01$; final $R^2 = .27$, $F(11, 1567) = 51.57$, $p < .001$.
*$p < .05$. **$p < .01$. ***$p < .001$.

Unit Effects on Posttraumatic Stress Disorder

A potential contributor to the above-described linear interaction is the influence of unit assignment. In other words, units as a whole may systematically vary in their levels of cohesion, making the cohesion-PTSD relationship for individual Army personnel contingent, in part, on unit assignment for each soldier. This possibility is suggested by multiple studies indicating a significant relationship between individually reported unit cohesion and unit assignment (see Griffith, 2002, for a review). A major grouping variable such as unit membership, when unacknowledged, can also result in significant increases in both Type 1 and Type 2 error rates for multiple regression results (Bliese & Hanges, 2004), even with the use of large samples (Barcikowski, 1981).

Following methodological suggestions by Hox (2002), an "intercepts-only" multilevel model was therefore constructed. Such a model is conceptually similar to a one-way ANOVA, with one critical difference being that the fixed ANOVA grouping variable is instead treated as a random factor in a regression analysis. For the purposes of this analysis, unit assignment at the battalion level was entered as a level 2 (i.e., grouping) variable in a multilevel model, and a covariance parameter estimate was calculated. This parameter estimated variance in PCL scores accounted for by unit assignment and was examined by means of a z test to determine if mean PCL scores for units varied more than would be expected by chance. Such an analysis provided a covariance parameter estimate of 1.40 (residual = 161.40), which was not statistically significant, $z = 1.15$, $p = .13$, one-tailed test. Calculation of the intraclass correlation (an estimate of effect size in multilevel model for the relationship between a level 2 predictor and a dependent variable) for unit assignment and PCL scores obtained a value of $\rho < .01$, indicating that less than 1% of variance in PCL scores in this sample is associated with unit assignment. Taken together, these results suggest that unit assignment, measured at the battalion level, was not a significant predictor of PTSD symptom levels in this sample.

DISCUSSION

This sample of military personnel reported moderate levels of PTSD symptoms, with a screening estimate of current PTSD of 10%. Thus, even using a stringent criterion for PTSD diagnosis, PTSD rates exceeded expectations for a noncombat, predominantly male, American group (i.e., a predicted weighted lifetime rate of 5.5%, according to documented male/female PTSD rates in the United States; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). Although differences in prevalence rates may vary by chance among samples, report of PTSD symptoms was linked to specific life experiences, suggesting that the increased prevalence is not attributable to artifact (e.g., participants reporting generalized distress that is not directly associated with a particular life event). This finding is consistent with epidemiological studies that have demonstrated high-exposure rates to premilitary stressors among military personnel (Hourani, Yuan, & Bray, 2003; Merrill et al., 1998; Stretch, Knudson, & Durand, 1998). Given research indicating that prior emotional disturbance increases stress vulnerability (e.g., King, King, Foy, & Gudanowski, 1996), this elevated rate of noncombat PTSD suggests that a subset of these service men and women may be at heightened risk for exacerbation of already existing PTSD during or after war-zone service.

Findings further suggest that, in addition to demographic variables, life experiences and perceived unit cohesion contribute independently to prediction of PTSD symptoms. Among demographic variables included in the regression, only age and ethnicity significantly predicted PTSD, with younger age and ethnic minority status contributing to heightened PTSD symptoms, when controlling for nondemographic variables. Prior stressful life events strongly predicted PTSD symptoms, supporting a dose-response relationship (Ozer, Best, Lipsey, & Weiss, 2003). Extending studies indicating that unit cohesion factors impact combat-related PTSD (Bowman & Yehuda, 2004); unit support and satisfaction with leadership significantly predicted noncombat-related PTSD symptoms in a military sample, even when controlling for demographic variables and life stressors. In addition, findings suggest that the association of stressful life events with PTSD symptoms decreases as unit cohesion increases, or, put another way, that the association of unit cohesion with PTSD symptoms increases as stressful life events increase. Consistent with study hypotheses, a curvilinear moderator effect was not found, suggesting that the levels of stressors typically associated with predeployment Army duty do not reach levels sufficiently severe as to overwhelm the positive coping function of high levels of unit cohesion. Thus, by both direct and indirect pathways, higher levels of unit cohesion appear to be particularly beneficial among individuals exposed to significant stress prior to their military careers. Such results have implications for both pre- and postdeployment healthcare, suggesting the potential importance of developing interventions that target perceived leadership and social support within military units.

Study limitations include derivation of PTSD diagnoses by self-report measure, the subjective nature of some life event items, and retrospective measurement of predeployment stressors. However, these limitations are balanced against a large sample of Army personnel who reflect a full range of military duties and occupational specialties and were examined prior to overseas deployment. Predeployment measurement of unit cohesion is especially helpful in that, it can serve in subsequent analyses as a relatively objective indicator of unit satisfaction prior to exposure to the stressors of combat. Reliance on postdeployment measurement of stressor levels and unit cohesion, without premilitary measures to serve as a baseline, cannot exclude the possibility than any observed curvilinear relationships are artifactual in nature. Simply put, it could be that individuals experiencing high levels of overwhelming symptoms engage in a biased reporting referred to by Brown (1974) as an "effort after meaning." Thus, this study provides key predeployment information highly relevant to disentangling these causal questions regarding the growing ground forces currently deployed overseas and suggests that substantial stress-related emotional symptoms may exist in military personnel prior to overseas deployment. Given the poor mental health outcomes associated with contemporary war-zone deployments (Hoge, Auchterloine, & Milliken, 2006), such preexisting symptoms may serve as vulnerabilities that are subsequently activated by war-zone deployment (Friedman, 2004). Yet, at least one potentially modifiable factor (unit cohesion) is associated with expression of stress-related symptoms, and interventions designed to increase unit cohesion may help ameliorate such vulnerabilities. Ongoing longitudinal efforts with this cohort promise to provide data relevant to the interplay between predeployment, war-zone, and postdeployment factors and their impact on mental health outcomes.

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PTSD and health functioning in a non-treatment seeking sample of Iraq War veterans: A prospective analysis

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Abstract—To evaluate the impact of posttraumatic stress disorder (PTSD) on health-related functioning, 800 U.S. Army soldiers were assessed before and after one-year military deployments to Iraq. As part of the Neurocognition Deployment Health Study procedures, each soldier completed at both time points self-report indices of PTSD symptom severity, health behaviors (smoking, alcohol use), and somatic health-related functioning. Participants also completed a health symptom checklist at post-deployment assessment. Structural equation modeling revealed that post-deployment PTSD severity was associated with change in somatic health functioning through post-deployment health symptoms as an intermediary variable. These relationships were independent of health risk behaviors, which had little association with somatic symptoms or PTSD. Findings highlight the functional impact of PTSD, which extends beyond psychological symptoms to health-related day-to-day functioning.

Key Words: functioning, health, health risk behaviors, Iraq War, OIF, PTSD, soldiers, veterans, VR-12

Abbreviations: PTSD = Posttraumatic stress disorder, VA = Veterans Affairs, OIF = Operation Iraqi Freedom, NDHS = Neurocognition Deployment Health Study, AD = Active Duty, NG = National Guard, PCL = PTSD Checklist, DSM-IV = Diagnostic and Statistics Manual, Fourth version, VR-12 = Medical Outcomes Study Short Form 12 in military veterans (VR-12, formerly referred to SF12V), SF36V = Medical Outcomes Study Short Form 36, PCS-12 = physical component summary of VR-12, SEM = structural equation modeling, FIML = full information maximum likelihood, MLR = maximum likelihood method with robust standard errors, CFI = comparative fit index, RMSEA = mean square error of approximation.

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INTRODUCTION

The clinical impact of posttraumatic stress disorder (PTSD) extends well beyond the more narrowly defined symptom criteria required by current diagnostic psychiatric taxonomy systems [1]. In addition to leading to a spectrum of psychological symptoms, PTSD is also associated with significant functional impairment, including increased risk of somatic symptoms and health disorders [2-7], health-related changes in day-to-day functioning [8-13], diminished overall well-being and quality of life [8,14-16], psychosocial and interpersonal dysfunction [17-19], and occupational impairment [17,20]. Such functional impairment, especially when health related, may result in significant costs to society [13,21]. For example, individuals with PTSD diagnosis use more medical services and incur higher health care costs compared to those with other psychiatric disorders [7,16,21-27]. Among health care consumers such as combat veterans who are at increased risk for PTSD [28-31], the personal burden and societal costs may reach unacceptably high levels.

Although mounting empirical evidence strongly suggests that higher levels of PTSD are associated with poorer health-related functional outcomes, less is known about potential mechanisms leading to health-related dysfunction in PTSD [32]. Increased knowledge of mechanisms through which PTSD leads to functional impairment (i.e., “mediators”) holds potential to influence early interventions targeting prevention of health-related functional impairment. Likewise, identification of mediators potentially helps identify PTSD subsets at elevated risk, thereby informing resource allocation.

Health symptoms and health risk behaviors may be particularly important mediators of the relationship between PTSD symptomatology and health-related functional outcomes. PTSD has been linked both to increased risk of somatic symptoms such as dizziness, fainting spells, pounding or racing heart, or shortness of breath [7,11,33-35] and to medical illnesses [11,36], such as cardiovascular disease [29,37-38], nervous system disease [39], and gastrointestinal disorders [10]. Although there may be several psychological [40-41] and biological [42-43] mechanisms explaining associations between PTSD and health outcomes [44], health risk behaviors such as alcohol use [5,45-46] tobacco use [5,9,47-48], and poor sleep hygiene [7,43] stand out as potentially modifiable risk factors for poor health outcomes in individuals expressing high levels of PTSD symptoms [49]. Less is known, however, about the impact of PTSD-related health risk behaviors and health symptoms on health functioning.

Efforts to examine relationships between health risk behaviors or health symptoms and functional outcomes in PTSD point to the role of both health behaviors and health symptoms in at least partially mediating the relationship between PTSD symptomatology and functioning, but remain inconclusive. For example, in comparison to population norms, a cohort of over 800 military veterans seeking treatment for PTSD at a VA facility showed increased health risk behaviors, increased chronic medical conditions, and poorer health-related functional outcomes [5]. Similarly, data from over 36,000 respondents surveyed as part of the Canadian Community Health Survey indicate that PTSD was associated with physical health problems, poor quality of life, and short- and long-term disability [50]. Among over 2000 adults residing in New York

City on the day of the World Trade Center attacks, excessive alcohol use was associated with both PTSD symptoms and poor mental health functional status [46].

In contrast, although alcohol use was high among patients who underwent surgery for physical traumas, it was not independently associated with functional outcomes, whereas PTSD diagnosis predictably showed strong independent associations with functional outcomes [45], suggesting a direct link between PTSD and functioning. Results of the VA Normative Aging study have suggested that PTSD may be associated with functioning independently of behaviors such as alcohol consumption and smoking [9], although links between smoking and functioning were also observed. Likewise, using cross-sectional data, Taft et al. [51] found that PTSD symptom severity was the most important variable explaining functional health status among both men and women in a sample of over 1600 Vietnam veterans enrolled in the National Vietnam Veterans Readjustment Study. Among male veterans, however, PTSD symptom severity was also linked to functional status via physical health conditions.

In one of the most comprehensive descriptions of causal pathways between PTSD symptoms and health functioning, Ford et al. (52) studied over 300 World War II veterans previously exposed to mustard gas. This cross-sectional study revealed several important findings: (1) toxic exposure affected health problems and health functioning through PTSD symptoms (i.e., PTSD mediated the relationship between exposure and health); (2) although PTSD symptoms were directly related to health functioning, physical health problems also affected functional status, and mediated the relationship between PTSD symptoms and health care utilization; and (3) alcohol use and smoking behaviors were not related to functional status or PTSD symptoms.

This paper extends the work of Ford et al. by addressing longitudinal relationships between PTSD symptomatology, health risk behaviors, health symptoms, and health-related functioning. Specifically, the study examined the relationship of post-deployment PTSD symptom severity to pre- to post-deployment change in physical health-related functioning in U.S. Army soldiers deployed to Iraq in support of Operation Iraqi Freedom (OIF). Additionally, two health-related factors (i.e., health risk behaviors and health symptoms) were examined as potential mediators of this relationship. The prospective study design, including pre- and post-deployment assessments, offered a unique opportunity to examine directional relationships with more rigor than that possible within cross-sectional frameworks or via longitudinal assessment beginning after trauma exposure. The non-treatment seeking sample of Iraq War veterans also provided a rare opportunity to examine relationships among PTSD symptoms, health risk behaviors, health symptoms, and health-related functioning in a recently trauma-exposed sample, prior to development of chronic dysfunction.

We hypothesized that PTSD symptom severity at post-deployment would be inversely related to change in physical health functioning. Such change was measured with “residualized” scores: the values of the post-deployment functioning outcome measure after removing the contributions of the pre-deployment scores to this measure (i.e., a difference score between predicted physical health functioning from the earlier assessment and the actual observed score at the later assessment). We further predicted that in addition to direct relationships between PTSD symptomatology and physical health-related functioning, the relationship between PTSD symptoms and physical health-related functioning would be partially mediated by health-related risk behaviors and post-deployment health symptoms. In addition, we took advantage of our assessments of pre-deployment PTSD, smoking, and drinking, and their associations with one another and with pre-deployment physical health functioning, to examine the stability of the pattern of their relationships over time.

METHODS

Human Subjects Considerations

Human subjects approvals were obtained from Human Subjects Review Boards of the Army, Tulane University Health Sciences Center, and Department of Veterans Affairs. All participants provided written informed consent prior to participation.

Participants

Participants were 800 U.S. Army soldiers who deployed to Iraq in support of OIF between October 2003 and December 2004 and were assessed before (Time 1) and after (Time 2) their deployment. Participants were selected from a cohort of 1542 soldiers enrolled in the Neurocognition Deployment Health Study (NDHS), a larger study targeting neuropsychological outcomes of Iraq deployment [53-54]. Detailed sampling, recruitment, and consent procedures are described elsewhere [54]. In brief, sampling was conducted at the battalion unit level and attempted to capture heterogeneous deployment experiences and geographic separation within the war zone. Units represented combat arms, combat support, and combat service support functions, and were drawn from both the regular active duty (AD) force and the National Guard (NG). Study volunteers were not invited to complete procedures if pending separation from service or reassignment to another installation at Time 1, or if unable to complete the study protocol due to physical limitations (e.g., broken hand).

The Time 1 NDHS participation rate (n = 1542) was high (94.4%). At Time 2, participants who remained assigned to units located at the same AD military installation or NG armory were again invited to participate in the full study protocol. Of the 1542 soldiers assessed at Time 1, 75.5% (70.8% from deployed units, 82.9% from non-deployed units) participated at Time 2. Because hypotheses center on relationships between war-related PTSD and health functional impact, only soldiers who deployed between Time 1 and Time 2 are considered in this report. At Time 2, the predominant reason for non-participation among deployers was that they were no longer with their original military unit (n = 186; 60.4%). Other reasons for non-participation at Time 2 included being on leave or special assignment (n = 36; 11.7%), sickness/injury (n = 7; 2.2%), deployed at Time 2 (n = 7; 2.2%); declined participation (n = 7; 2.2%); de-activated Reservist (n = 4; 1.3%); deceased (n = 3; 1.0%); and other/unknown (n = 58; 18.8%). An additional 24 deployers were excluded for invalid (i.e., internally inconsistent) questionnaire response profiles (n = 21) or not completing a questionnaire at both time points (n = 3), resulting in a final deployed sample of 800 (n = 687 AD; n = 113 NG) soldiers.

At Time 1, participants in the final sample generally reflected the broader OIF-deployed Army population. On average, participants were 25.8 years (SD = 6.0 years) of age, had completed 12.5 years (SD = 1.4 years) of education, and had served in the Army 4.7 years (SD = 4.9 years). Almost half (46.9%) were married at Time 1, and

38.6% identified themselves as being of ethnic minority status. Women (7.0%) were under-represented compared to the expected proportion of contemporaneously deployed Army women, but were representative of the gender composition of participating military units. Commissioned officers were also under-represented at 2.2%. At Time 1, 11.5% had participated in a prior overseas operational deployment (1.3% deploying to Afghanistan or Kuwait in 2001 or later; n = 1 participant having served in Iraq). The most prevalent military occupational categories were infantry/gun crew (37.0%), communication/intelligence (16.5%), electrical/mechanical equipment repair (15.1%), and service supply (8.1%). Among participants for whom deployment and redeployment dates were available (*n* = 777), all but 27 (23 AD, 4 NG) served a 12-month OIF rotation.

Measures

Demographic (e.g., age, gender) and military (e.g., rank, deployment history) information was queried via interview and written survey questions. Military information was verified by service records. Comprehensive description of primary assessment data and secondary data obtained from automated military databases is described elsewhere [52]. Description of measures relevant to hypotheses in this report follows.

PTSD symptom severity. The PTSD Checklist (PCL), a widely-used self-report scale measuring distress levels associated with each DSM-IV PTSD symptom [55-56], was used to derive PTSD symptom severity scores and was administered at both Time 1 and Time 2. The civilian version was used for comparability across time points, including Time 1 in which the majority of participants had no prior combat exposure. The PCL is characterized by high test-retest reliability (*r*s = 0.92 and 0.88 for immediate and 1-week retest, respectively), internal consistency (Cronbach's alpha = 0.94), and convergent validity (*r*s > 0.75) with other PTSD measures [57]. Dimensional symptom-based indicators of PTSD (i.e., re-experiencing, avoidance, emotional numbing, hyperarousal), reflecting a 4-factor model [58], were generated by grouping PCL items into appropriate subscale scores.

Health risk behaviors and health symptoms. To reduce respondent burden, health risk behaviors were limited to screening items judged to be of highest relevance to NDHS primary outcome domains (neuropsychological functions). Collected at Time 1 and Time 2, health risk measures included average number of alcoholic drinks per week in the month prior to assessment and current cigarette smoking. Smoking was categorized as 0 = no smoking, 1 = smokes less than 1 pack per day, 2 = smokes 1-2 packs per day, 3 = smokes 3 or more packs per day, subsequently collapsed into no-smoking (0) and smoking (1).

Health symptoms were measured at Time 2 with an abbreviated version of a health symptom checklist, adapted from earlier work involving 1991 Gulf War veterans [59]. Each participant was asked to report the frequency that he/she experienced a set of 17 health symptoms and complaints (e.g., headaches, irregular heart beats, common cold) over the prior 30 days, scaled from 0 to 4 (0 = no symptom; 1 = rarely, 1-2 times in all; 2 = some, about once per week; 3 = often, several times per week; 4 = very often, almost every day). The summary score was computed by summing the 17 symptom frequencies.

Health-related functioning. The self-appraised impact of somatic ("physical") problems on basic components of day-to-day functioning (e.g., accomplishing less than usual) were measured at Time 1 and Time 2 with the physical component score (PCS-12) of the Medical Outcomes Study Short Form 12 [60], adapted for use in military veterans (VR-12, formerly referred to SF12V). The VR-12 is the short form of the widely used SF36V. PCS-12 (short form) component score have correlated highly with PCS-36 scores (*r* = 0.95) from the SF36 (long form) [60]. Alternate forms reliability measures have shown estimates from 0.84 to 0.90 across different samples varied by age, gender, and health status [61]. Test-retest reliability, based on intraclass correlations, has been high for healthy community volunteers (r = 0.84) [62] and volunteers with severe mental illness diagnoses (r = 0.79) [63].

Procedures

As described by Vasterling et al. [54], survey measures were administered in small groups at military installations for most participants. It was also possible to contact a smaller subset of participants (*n* = 21) by mail who were not present at military installations during Time 2 data collection. Time 1 assessments for deploying military units occurred between April 2003 and July 2004. Face-to-face Time 2 assessments occurred between January 2005 and September 2006, with mail assessments completed by December 2006.

Pre-deployment assessment of AD soldiers occurred an average of 95.2 days (SD = 95.1 days) prior to actual deployment (median = 45 days), although most participants thought deployment to be imminent at the time of their assessments. The discrepancy between expected and actual deployment dates reflects that a subset of AD participants belonged to military units for which deployment orders were cancelled after their Time 1 assessment. Deployment orders for these units were subsequently reinstated. Thus, although all units were actively preparing to deploy at Time 1, a subset did not actually deploy until several months later.

At Time 1, NG soldiers had been recently mobilized from their home states and sent to Camp Shelby for training and preparation. The NG pre-deployment assessments immediately preceded participation in intensive desert training, which was followed by a brief return to Camp Shelby, and then deployment to Iraq. Reflecting this sequence of events, pre-deployment assessment of NG soldiers occurred an average of 114.3 days (SD = 31.9 days) prior to their overseas deployment (median = 115 days).

Post-deployment assessment of AD soldiers serving full tours occurred an average of 73.4 days (SD = 19.5 days) from each participant's return from Iraq (median = 75 days); post-deployment assessment of NG soldiers occurred an average of 197.5 days (SD = 34.0 days) following their return from Iraq (median = 189 days), reflecting scheduling constraints associated with the timing of NG post-deployment assemblies.

Statistical Analyses

Data Preparation. Missing values for specific items (occurring in <3% of cases) were replaced by the mean value of the individual's completed items for that measure; however, if fewer than 50% of the items on a measure were completed, summary scores were not computed.

Analyses. For all analyses, raw data were submitted to the Mplus program version 4.1 [64]. Prior to computing the multivariate models, an estimated bivariate correlation matrix of the latent study variables was examined and interpreted according to Cohen [65]. Structural equation modeling (SEM) was used to test the hypothesized models. Data were collected and therefore clustered within battalion-level units. To account for the effects of assignment to a particular battalion, battalion unit membership was entered as a cluster variable into all SEM equations. Age was included as a covariate in all SEM analyses. The full information maximum likelihood (FIML) method was used to accommodate missing data (occurring in 14% of cases). Soldiers who did not participate in the post-deployment assessment were excluded from analyses.

PTSD was modeled as a latent variable with four observed indicators: PTSD re-experiencing, PTSD avoidance, PTSD numbing, and PTSD hyperarousal subscales. Age was included in the measurement model as an observed variable. The model also involved the following variables that were singly-identified by their corresponding observed scale scores: pre-deployment smoking, pre-deployment drinking, pre-deployment physical functioning, post-deployment smoking, post-deployment drinking, post-deployment health symptoms, and post-deployment physical functioning,

SEM analyses followed a two-step approach. First, a measurement model was computed to test the adequacy of the hypothesized latent (i.e., not directly observed) variables in explaining the corresponding observed indicators. Second, a structural model was specified and evaluated to examine the effects of PTSD symptoms, negative health behaviors, and health symptoms on physical functioning. Variables from pre- and post-deployment time periods were used to test the hypothesized model pathways, with the exception of health symptoms for which data were collected only at post-deployment. Mplus was used to calculate the direct and indirect effects of model predictors on physical functioning. The two-wave (pre- and post-deployment) data structure enabled us to examine whether model predictors influenced change in functioning over time and to ascertain the stability of predictors over the pre- to post-deployment interval.

All model variables were continuous with the exception of pre- and post-deployment smoking, which was modeled dichotomously (smoker vs. non-smoker). Mplus model pathways involving dichotomously modeled variables are based upon polychoric correlation coefficients [66]. Given that the smoking variable was dichotomous, the weighted least-squares with mean and variance adjustment (WLSMV) estimator, which has been shown to be an ideal estimator for models involving dichotomous data [67], was used in all SEM analyses.

RESULTS

Variable Descriptives and Bivariate Correlations among Study Variables

Table 1 provides the means and standard deviations of key study variables at pre- and post-deployment assessment. Results of bivariate correlational analyses revealed significant bivariate correlations in the hypothesized direction for most model latent variables (**Table 2**). Correlations between health risk behaviors (smoking and drinking) and other model variables were generally in the small range according to Cohen's guidelines [65]. The cross-sectional correlation between PTSD and physical functioning was small at pre-deployment and moderate at post-deployment. In contrast, post-deployment health symptoms evidenced a large correlation with post-deployment PTSD and a moderate to large correlation with post-deployment physical functioning. As would be expected, post-deployment values of key measures (PTSD, health behaviors, functioning) were strongly correlated with pre-deployment values of the same measures. This was particularly true of smoking status, which changed very little over time.

Multivariate SEM Analyses

SEM was used to test the hypothesized multivariate model involving PTSD symptoms, health risk behaviors, health symptoms, and physical functioning at pre- and post-deployment (**Figure 1**).

Measurement model. A measurement model was first calculated to determine the adequacy of the hypothesized latent model structure in explaining the underlying observed data. The measurement model was shown to produce an acceptable model fit. Although the chi-square test was significant (χ^2 (5, N = 800) = 14.37, p = .01), this test is shown to be extremely sensitive to even small model-data deviations with large samples and is, therefore, a poor measure of the overall statistical model [68]. Therefore, the comparative fit index (CFI) [69] and root mean square error of approximation (RMSEA) are more appropriate fit indices by which to judge model fit. The CFI was .98, exceeding the recommended standard of .95, and the RMSEA estimate of .05 fell below its suggested maximum value of .08 [70-72]. These results suggested that the latent variable model effectively matched the underlying data structure.

Structural model. A structural model was next computed to test the hypothesized relationships among study variables (**Figure 1**). Fit indices for the structural model suggested an acceptable fit to the data, (χ^2 (5, N = 800) = 16.53, p = .006), CFI = .98, RMSEA = .05.

Pre-deployment. At pre-deployment, more severe PTSD symptomatology was associated with greater alcohol consumption, but the relationship between PTSD symptoms and smoking behaviors was nonsignificant (**Figure 2**). Endorsement of pre-deployment smoking was associated with poorer pre-deployment physical health functioning, whereas level of drinking was not related to physical functioning at the pre-deployment assessment. In addition, pre-deployment PTSD symptomatology was negatively associated with pre-deployment physical health functioning.

Post-deployment. At post-deployment, PTSD symptoms were again directly associated with drinking behavior. Moreover, this relationship was maintained even after controlling for pre-deployment drinking, suggesting that higher levels of post-deployment PTSD were associated with increases in drinking from pre- to post-deployment. A large positive relationship was also observed between post-deployment PTSD and post-deployment health symptoms. In contrast to a direct relationship between PTSD symptoms and health functioning observed at pre-deployment, the association between post-deployment PTSD symptoms and change in physical health functioning across deployment was found to be indirect (**Figure 2**). Specifically, the relationship between PTSD and functional change was almost entirely explained by post-deployment health symptoms (standardized indirect effects = -.27, p < .001). In the presence of PTSD, neither post-deployment drinking nor post-deployment smoking behaviors were associated with post-deployment health symptoms or physical health functioning (**Table 3**). Hence, changes in pre- to post-deployment physical health functioning were partially explained by the positive pathway from post-deployment PTSD to health symptoms and by the negative pathway from health symptoms to residualized change in physical health functioning.

DISCUSSION

To our knowledge, this is the first study to examine longitudinal relationships between PTSD symptomatology and health-related functioning. In a sample of 800 US Army soldiers deployed to Iraq, we found an indirect relationship between PTSD and health-related functional outcomes. Specifically, post-deployment PTSD symptom severity was only weakly related to day-to-day health related functioning if the influence of health *symptoms* was controlled. Instead, PTSD symptoms seem to adversely impact physical health functioning via their negative effect on health symptoms, which in turn negatively influence day-to-day functioning. While intuitive that the impact of health on day-to-day functioning has much to do with the number and frequency of somatic symptoms, of particular relevance to military veterans and other trauma victims seeking treatment for PTSD, such health symptoms appear to be set in motion by PTSD.

Contrary to our hypotheses, the statistical model revealed no evidence that select health risk behaviors served as a mediator between PTSD symptoms and health symptoms. Although smoking mediated the relationship between PTSD and health functioning at pre-deployment, smoking was not related to either PTSD symptoms or health functioning at post-deployment. Instead, smoking status appeared to be relatively invariant across time, regardless of PTSD symptom levels or health functioning status. Therefore, neither the direct relationship between PTSD symptoms and health symptoms nor the indirect relationship between PTSD and decline in health functioning (mediated by health symptoms) could be explained by health risk behaviors.

This finding suggests a more direct relationship, or the existence of an unobserved mediating factor, between PTSD and health symptom development. There are several alternate mechanisms, such as depression [74], coping behaviors [75], and biological resiliency factors [76], that have been proposed but not tested within our model. Alternately, it may be that our measurement of behavioral health risk factors, which was limited to relatively course screening measures, did not capture the most relevant dimensions of health risk behavior.

It is also noteworthy that relationships between PTSD symptoms, health symptoms, and day-to-day functioning were demonstrated in a cohort of non-treatment seeking, predominantly young Army soldiers who had recently returned from overseas deployment. It could be hypothesized that such relationships might be even more prominent among treatment-seeking military veterans or among those beginning to express more chronic symptoms of PTSD. That PTSD symptoms were already appearing to exert some impact on health-related functioning in a population that should not otherwise be at heightened risk for diminished health status also highlights the benefits of early mental and physical health screening in both primary care and mental health settings, even among seemingly healthy newly returning veterans. Finally, these findings point to the need for early mental health interventions to take into consideration health symptoms and functional impact. Such outcomes as quality of life, psychosocial relationships, and occupational functioning are equal in importance as intervention targets to more traditional symptom relief.

Interpretation of study findings is limited by several factors, including the failure to measure somatic health symptoms at pre-deployment assessment, the restriction of health risk assessment to screening measures, the under-representation in the sample of women, officers, and reservists, and the inclusion of only one service branch. Nonetheless, the prospective design, large sample size, range of military occupational specialties, and the representativeness of the sample to the larger deployed Army population on other relevant dimensions provide examination of relationships among PTSD symptoms, health, and functioning in a manner not previously possible.

CONCLUSION

This prospective study of a large cohort of US Army soldiers who deployed to Iraq in support of OIF revealed that the impact of PTSD extends beyond adverse emotional sequelae to health symptoms and health-related day-to-day functioning. The findings have significant implications for the reduction of personal burden and societal costs among military veterans and other trauma-exposed populations who develop PTSD symptoms following exposure to extreme stress.

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Table 1.
Descriptive statistics (mean ± standard deviation) of observed SEM model variables for deployed soldiers who participated in pre- and post-deployment assessments (*N* = 800).

Variable	Time 1	Time 2
PCL re-experiencing summary score	7.68 ± 3.88	9.38 ± 4.43
PCL avoidance summary score	3.47 ± 2.04	3.85 ± 2.17
PCL numbing summary score	8.13 ± 3.85	8.46 ± 4.05
PCL hyperarousal summary score	9.32 ± 4.16	11.06 ± 4.87
PCL summary score	28.60 ± 12.04	32.70 + 13.47
% current smoker	48.9%	48.4%
alcoholic drinks per week, past month	7.51 ± 11.52	8.29 ± 10.61
VR-12 physical component score	51.99 ± 6.90	50.51 ± 7.57
Health checklist summary score	--	13.40 ± 11.59

SEM = structural equation model; Time 1 = pre-deployment; Time 2 = post-deployment; PCL = PTSD Checklist

Table 2.
Estimated SEM latent variable correlations.

Variable	1	2	3	4	5	6	7	8	9	10
1. T1 age	---									
2. T1 PTSD	-0.12*	---								
3. T1 smoking	-0.09*	0.10*	---							
4. T1 drinking	-0.11*	0.09*	0.27*	---						
5. T1 phys function	-0.11*	-0.16*	-0.10*	-0.03	---					
6. T2 PTSD	0.03	0.52*	0.04	0.12*	-0.13*	---				
7. T2 smoking	-0.12*	0.09*	0.92*	0.23*	-0.07*	0.10*	---			
8. T2 drinking	-0.15*	0.12*	0.23*	0.57*	0.00	0.12*	0.31*	---		
9. T2 health symptoms	0.08*	0.40*	0.06	0.01	-0.20*	0.65*	0.05	0.06	---	
10. T2 phys function	-0.12*	-0.16*	-0.04	-0.01	0.35*	-0.26*	-0.05	-0.03	-0.40*	---

T1= pre-deployment, PTSD = posttraumatic stress disorder, smoking (0= non-smoker, 1=smoker), drinking = alcoholic drinks per week, phys function = physical functioning, T2 = post-deployment. Relationships involving smoking are based upon polychoric correlations. * *p* < .05.

Table 3
SEM model standardized effects of post-deployment model predictors on post-deployment physical health functioning while controlling for pre-deployment physical health functioning.

Variable	Direct Effects	Indirect Effects	Total Effects
Post-deployment smoking	.00	-.02	-.02
Post-deployment drinking	-.02	.01	-.01
Post-deployment PTSD	.06	-.28***	-.22***
Post-deployment health symptoms	-.40***		-.40***

Neuropsychological Functioning and Posttraumatic Stress Disorder: Implications for War-Zone Veterans

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Austere and stressful circumstances, including exposure to horrific and life-threatening situations, typically characterize war zones. Both human and animal studies have provided considerable scientific evidence that exposure to extreme stress of the type encountered in war zones can lead to adverse neurobiological and psychological sequelae, including pronounced psychiatric symptoms and maladaptive behavioral changes. Unfortunately, it is becoming increasingly apparent that the consequences of war and other psychological trauma can extend well beyond classic psychiatric symptoms to include other types of health-related and psychosocial problems. Neuropsychological functioning encompasses cognitive (e.g., memory, attention, and reasoning), perceptual-sensory-motor (e.g., motor speed), and emotional (e.g., mood) behaviors thought to reflect brain integrity. In this paper, we discuss the neuropsychological correlates of trauma exposure, particularly among war zone veterans, and the implications of these findings for prevention, health care, and the research agenda. Specifically, this paper reviews the occupational and functional consequences of trauma exposure and describes both the arguments supporting and factors limiting the implementation of neuropsychological screening assessments as standard health surveillance among military populations.

Epidemiology of trauma exposure and PTSD

Psychological trauma is typically defined as an experience that poses a serious threat to the life or physical integrity of the individual or someone close to him or her. Trauma of this nature is often accompanied by an intense emotional reaction. Examples include physical and sexual assault, child abuse, fires and other natural disasters, terrorist attacks, life-threatening accidents, community violence, and military combat. At least one out of two people will be exposed over the course of their lifetimes to a psychologically traumatic event, and over half of those exposed to psychological trauma will be exposed to multiple traumatic events[1]. The rate of exposure increases in populations at high risk, such as military personnel deployed to war zones.

Exposure to psychological trauma results in a physiological and psychological stress response thought to be immediately adaptive during life-threatening situations. This response helps the organism take appropriate action and therefore enhance the odds of survival. Posttraumatic stress disorder (PTSD) can develop , however, when acute stress responses occurring in the immediate context of the life-threatening situation endure after the threat is removed and become chronic symptoms. The symptoms of PTSD include re-experiencing of the trauma (e.g., nightmares, intrusive thoughts), avoidance of thoughts and environmental stimuli reminiscent of the trauma, emotional "numbing", and increased incidence of arousal (e.g., difficulties with sleep, exaggerated startle). The lifetime prevalence of PTSD in the adult U.S. population has been estimated to be 6.8%, with the 12-month prevalence rate estimated to be 3.6%[1, 2]. PTSD occurs much more frequently in populations in which trauma exposure is more common and severe, such as war-zone veterans. For example, a recent re-analysis of the National Vietnam Veterans Readjustment Survey yielded a conservative estimate that 18.7% of Vietnam veterans experienced PTSD at some point in their lives, and 9.1% met criteria for current PTSD over ten years after their war-zone service[3]. Although not derived from population-based samples, recent screening estimates of current PTSD among Iraq War veterans have suggested that over 12% of veterans of contemporary war zones experience clinically significant posttraumatic stress symptoms within the first 90 days of their return[4], with the prevalence of the disorder increasing over time[5].

Neuropsychological functioning and PTSD

Subjective complaints of cognitive impairment among those affected by exposure to severe stress are not uncommon, as reflected by the integration of attention and memory abnormalities into the PTSD diagnostic criteria. These symptoms include poor concentration, "hypervigilance" (i.e., enhanced attention) to threat, intrusion of distressing trauma-related memories into conscious thoughts and dreams, and psychogenic amnesia (i.e., certain aspects of the traumatic event cannot be readily recalled). These clinical expressions of cognitive abnormalities are echoed within two bodies of scientific research involving humans. In one area of research, studies have documented how people experiencing PTSD preferentially process trauma-relevant information as compared to information not perceived to be threatening. In the second research domain, observational studies have revealed performance decrements on specific types of emotionally neutral neuropsychological tasks. Not reviewed in this paper, but also of relevance, is a large body of analog research conducted with animals that suggests at least transient changes in learning and memory following stress exposure. We focus below on the evidence derived from studies involving humans exposed to traumatic events.

Information processing biases

Consistent with the clinical phenomenon of hypervigilance to potential environmental threat, PTSD is associated with biases in how threat-relevant information is processed[6]. People with PTSD are more likely to attend to, and to remember, trauma-relevant information than other types of information that is less personally threatening[7, 8]. There also is preliminary evidence that individuals with PTSD are biased to interpret emotionally ambiguous information as threatening under certain conditions[9].

The tendency in PTSD to attend to threat-relevant information has been especially well documented using an experimental paradigm known as the emotional Stroop task. The emotional Stoop task involves performing a perceptual task (i.e., naming the color of ink in which a word is printed) when the semantic content of words is potentially distracting because of their emotional relevance. Individuals with PTSD typically name the color of ink in which trauma-related words are presented more slowly than they color-name emotionally neutral or trauma-irrelevant word[10]. The slowed color-naming performance of individuals with PTSD is interpreted as reflecting greater interference imparted by the threat value of these words. The experimental finding of attentional bias resembles very closely the distraction that people with PTSD report when they are confronted with elements in their immediate environment or internal thoughts that remind them of the trauma.

Although not as extensively studied, there is also evidence of threat-relevant anterograde memory biases in PTSD. Anterograde memory refers to the process of learning and remembering new information. When presented with words that vary in their threat-relevance, trauma-exposed individuals with PTSD show enhanced recall of the trauma-related words whereas those without PTSD do not. This finding is especially true when memory is tested with free recall tests (i.e., recall without prompts)[11]. On memory tasks that require recall of a person's prior life events (i.e., autobiographical memory tasks), individuals with PTSD produce "overgeneral" memories in which they recall only broad categories of events, rather than specific detailed accounts of life events[11, 12].

When placed within an evolutionary context, information processing biases to threat-relevant information are initially adaptive. The cognitive capacity of any individual is limited, leading to ongoing prioritization of cognitive effort and resources. What this means is that we cannot attend to, or process with equal effort, all possible stimuli or events in our environments. How we allocate cognitive resources can therefore influence survival when we are confronted with life threat. In a potentially dangerous situation, it could be argued that survival will be enhanced if the source of danger is held in focus enough to take appropriate action. Selective memory of information relevant to previous threats can likewise help influence future behavior if the individual is again confronted by the threat. Unfortunately, initially adaptive cognitive responses to threats may be perpetuated beyond dangerous contexts and crossover to normal life. In the case of PTSD, this occurs even when such thought processes are no longer necessary and instead have become maladaptive.

Neuropsychological abnormalities on emotionally neutral tasks

Examination of neuropsychological abnormalities on emotionally neutral tasks remains a developing area of research. Learning, memory, attention, and intellectual functioning have been among the most commonly studied neurocognitive domains in PTSD samples, with learning and memory studies constituting the largest proportion of these studies[13]. Overall, this growing body of research indicates that PTSD is associated with mild deficits on learning and memory tasks, especially during the initial acquisition phases of learning, on tasks assessing specific components of attention, and on intellectual tasks assessing verbal abilities[14]. This emerging field is not without controversy, however, and some studies have not found neuropsychological abnormalities specific to PTSD[15-17].

Nevertheless, the evidence for anterograde memory dysfunction in PTSD is robust. A recent meta-analysis that aggregated data from more than 1,400 participants provided strong evidence that PTSD, as compared to the absence of PTSD comparators, is associated with less proficient memory for emotionally neutral material[18]. Despite considerable variability between studies, both civilian and military samples of adults with PTSD showed a consistent decrement in memory performance that was small to moderate in magnitude and concerned primarily with verbal rather than visual memory. Examination of concurrent conditions revealed that PTSD-related memory deficits could not be attributed to head injury, a condition with particularly high relevance to Iraq War veterans due to their elevated risk of exposure to road bombs and other blasts resulting in concussive injuries[19-20].

There is also significant evidence of attentional impairment associated with PTSD. In particular, PTSD has been associated with performance deficits on tasks that require working memory (i.e., the ability to manipulate information mentally) or the ability to maintain optimal levels of vigilance consistently over a prolonged interval (“sustained attention”)[21-23]. In contrast, other aspects of attention, such as the ability to shift focus, appear impervious to PTSD[23]. Interestingly, PTSD has been associated with cognitive disinhibition and commission errors across both attention and memory tasks, a pattern collectively suggestive of a failure to screen out task-irrelevant information[21]. Such a cognitive gating failure can be invoked to explain the failure to inhibit unwanted and distressing re-experiencing of the trauma, one of the hallmark symptoms of PTSD. In other words, people with PTSD are not always able to ignore upsetting information related to their trauma experiences.

Although few studies have comprehensively measured intellectual functioning in PTSD, those that have suggest that individuals without PTSD as compared to trauma-exposed individuals with PTSD tend to perform better on IQ tests, especially on those assessing verbal skills[17, 22, 24-26]. The dissociation between verbal and visuo-spatial performances on intellectual tasks[27] mirrors the pattern of relative verbal weaknesses on learning and memory tasks, pointing to potential functional brain asymmetries in the direction of the left cerebral hemisphere being relatively less activated than the right.

Neuropsychological functioning, stress, and the Iraq War

There is currently little published work addressing the neuropsychological outcomes of the Iraq War; however, we have recently published the results of a large scale study examining neuropsychological outcomes of contemporary war-zone participation[28, 29]. In this study, we used prospective methodology to document changes occurring from pre-deployment to post-deployment among over 600 Iraq-deployed Army soldiers and a comparable group of over 300 non-deployed Army soldiers. The results indicated that deployment to Iraq was associated with performance disadvantages on objective tests of learning, memory, and attention, and performance advantages on a test of simple reaction time. There is an elevated risk of concussive brain injury associated with deployment to Iraq; however, examination of the potential contributions of brain injury to the neuropsychological findings revealed that the findings could not be explained by deployment-related brain injury. Although PTSD symptoms could similarly not explain the deployment-related findings, the results are consistent with the pattern that might be expected to accompany a neurobiological stress response. The pattern of results suggested to us that the neuropsychological findings represented an arousal-based stress response that precedes PTSD symptoms but that may eventuate in PTSD if perpetuated.

Cognitive deficits and PTSD: Functional implications

In considering the clinical significance of neuropsychological abnormalities associated with war-zone stress and PTSD, the potential impact of cognitive impairment on daily functioning is the correlate of PTSD that is perhaps of greatest relevance to the individual and to society. Evidence that PTSD leads to decreased occupational functioning[30], reduced quality of life[31], and increased health risk[32,33] is accumulating. Although little work has been done to assess the specific functional impact of cognitive abnormalities in PTSD, cognitive impairment has potential to negatively impact work performance and other aspects of quality of life.

Cognitive deficits, for example, have been associated with negative employment outcomes following brain injury [34], including high rates of unemployment[35,36], frequent termination from jobs, and decreased work efficiency[37]. Schizophrenia studies have similarly revealed that neurocognitive functioning exerts a more potent effect on work capacity than do the more overt and often salient psychiatric symptoms associated with the disorder[38]. Even in healthy populations, cognitive impairment negatively affects occupational functioning via mechanisms such as reduced performance efficiency, compromised decision-making, distractibility, and increased error rates[39-44].

As a correlate of the potentially chronic neurobiological abnormalities associated with the stress response, neuropsychological deficits may also reflect a prodrome or surrogate for stress-related somatic illnesses. For example, allostatic load models of disease hold that an organism adapts to stress by directing energy to achieve biological stability. After going through repeated cycles of such adaptation, there can be a physiological cost, including the failure to “shut off” certain neurobiological responses that, when prolonged, can result in decreased immunity, tissue injury, and other adverse physiological effects such as elevated blood pressure and hormonal disruption[45]. If neuropsychological impairment indeed reflects neurobiological dysfunction associated with adaptation failures, these neuropsychological deficits may indicate the initial progression to a much more extensive array of health problems than cognitive compromise alone.

Cognitive deficits and PTSD: Policy implications

Healthcare, prevention, and surveillance in military and military veteran populations

The potential implications of neuropsychological compromise to the health and functioning of war-zone veterans suggests that neuropsychological screening assessments could be an important addition to standard health surveillance among military populations. In addition to the relevance of neuropsychological functioning to stress-related conditions, neuropsychological functioning is also sensitive to other potential deployment exposures such as some classes of environmental hazards and traumatic brain injury. An additional advantage of neuropsychological assessments as a measure of brain integrity is that they can be conducted without physical discomfort, invasive methods, or expensive technology. Moreover, neuropsychological functioning can be measured using standardized, performance-based instruments that result in reliable and objective measurement. The neuropsychological assessment process is a therefore a safe, portable, reliable, and cost-effective means of estimating neural health.

There are currently several limiting factors to the widespread implementation of standard neuropsychological surveillance in military and military veteran populations. First, neuropsychological evaluations can be time-consuming and may therefore be limited in feasibility, especially in times of increased demands on military personnel. Screenings are a viable alternative; however, the field is at a point of development in which significant work still needs to be done to assess the diagnostic efficiency of neuropsychological screening evaluations against more comprehensive "gold-standard" assessments in healthy, military populations[46]. A second and related impediment is that databases providing population-based normative data on neuropsychological screening batteries are scarce, making it difficult to effectively and appropriately interpret data derived from screening batteries. Finally, the widespread use of neuropsychological screenings implies the existence of an infrastructure, including sufficient healthcare providers with neuropsychological expertise that can handle referral of positive screens to the subsequent levels of assessment and/or intervention. The large potential gains in prevention and healthcare that can be realized through the implementation of neuropsychological screening, combined with the large numbers of currently deployed service members, highlight the immediate need to develop the appropriate normative work and healthcare infrastructure to facilitate clinically meaningful neuropsychological surveillance.

Implications for PTSD treatment research

There is a growing trend in treatment outcome and clinical trials research to define outcomes more broadly than symptom alleviation. Given the practical implications of neuropsychological integrity on day-to-day functioning, neuropsychological measures are a potentially valuable ancillary index of treatment success. Measurement of neuropsychological functioning as a treatment outcome may be especially relevant among returning veterans with polytrauma conditions, many of which involve both PTSD and traumatic brain injury. Similarly, inclusion of neuropsychological and information processing measures can inform mechanistic intervention research with relevance to both the neural substrates and cognitive mechanisms underlying the clinical expression of PTSD.

Neuropsychological assessment also has the potential to be used to examine individual differences as predictors of treatment response, adherence, and completion. Although treatments might show generally positive efficacy across large groups of people, not all individuals respond to treatments similarly. Biological variation (reflected in neuropsychological measures) may interact, for example, with psychopharmacological interventions in determining outcomes. Similarly, certain psychological interventions, particularly those with strong cognitive components (e.g., cognitive processing and cognitive-behavioral interventions), may be more or less effective depending on the cognitive strengths and weaknesses of the individual. Certain types of cognitive deficits, such as forgetfulness, could potentially affect adherence to many different types of treatment. Therefore, the effectiveness of a number of interventions will potentially be enhanced with memory aids, suggesting the need for systematic research targeting protocol modifications that will increase adherence to, and completion of, promising interventions via improving memory. To our knowledge, inclusion of cognitive predictors of treatment response is a vastly understudied area that has significant potential to contribute to optimized service delivery.

Conclusions

In summary, it has become increasingly clear that war-zone participation and other exposures to extreme stress can result in an array of psychiatric symptoms and functional impairments, including neuropsychological abnormalities. PTSD-related neuropsychological dysfunction highlights the breadth of stress-related sequelae and underscores the importance of looking beyond emotional distress in trauma-exposed individuals. Because of the direct relevance of neuropsychological functioning to occupational performance and other aspects of daily living, neuropsychological assessment is a potentially important healthcare tool that can be used to assist in recovery and treatment efforts. Specifically, neuropsychological assessment can help guide providers in their decisions about whether to initiate ancillary health care services such as cognitive and vocational rehabilitation, or whether modification of standard PTSD treatments is needed to accommodate any cognitive limitations. Finally, as a cost-effective indicator of brain integrity and cognitive resources, neuropsychological assessment stands to inform neurobiological and cognitive models of PTSD, contributing knowledge regarding mechanisms of treatment and which individuals might best benefit from various available treatment options.

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