ORIGINAL ARTICLE

Association of Time Since Deployment, Combat Intensity, and Posttraumatic Stress Symptoms With Neuropsychological Outcomes Following Iraq War Deployment

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Context: Previous research has demonstrated neuropsychological changes following Iraq deployment. It is unknown whether these changes endure without subsequent war-zone exposure or chronic stress symptoms.

Objective: To determine the associations of time since deployment, combat intensity, and posttraumatic stress disorder (PTSD) and depression symptoms with longer-term neuropsychological outcomes in war-deployed soldiers.

Design: Prospective cohort study involving (1) soldiers assessed at baseline (median, 42 days prior to deployment) and following return from Iraq (median, 404 days after return and 885 days since baseline), and (2) soldiers more recently returned from deployment assessed at baseline (median, 378 days prior to deployment) and following return from Iraq (median, 122 days after return and 854 days since baseline assessment).

Setting: Active-duty military installations.

Participants: Two hundred sixty-eight male and female regular active-duty soldiers (164 with 1-year follow-up; 104 recently returned).

Main Outcome Measures: Neuropsychological performances (verbal learning, visual memory, attention, and reaction time).

Results: There was a significant interaction between time and PTSD symptom severity (B=−0.01 [unstandardized], $P=.04$). Greater PTSD symptoms were associated with poorer attention in soldiers tested at 1-year follow-up (B=0.01, $P=.03$) but not in recently returned soldiers. At 1-year follow-up, mean adjusted attention error scores increased by 0.10 points for every 10 points on the PTSD scale. Greater combat intensity was associated with more efficient postdeployment reaction-time performances, regardless of time since deployment (B=0.48, $P=.004$), with mean adjusted reaction efficiency scores increasing by 4.8 points for every 10 points on the combat experiences scale. Neither depression nor contextual variables (alcohol use and deployment head injury) were significantly related to neuropsychological outcomes.

Conclusions: In this study of army soldiers deployed to the Iraq war, only PTSD symptoms (among soldiers back from deployment for 1 year) were associated with a neuropsychological deficit (reduced attention). Greater combat intensity was associated with enhanced reaction time, irrespective of time since return.

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In response to cognitive problems reported by veterans following previous wars,[1-4] the Neurocognition Deployment Health Study[5,6] was initiated to examine the neuropsychological outcomes of Iraq war deployment. Results of earlier assessment waves (predeployment/immediate postdeployment) suggested that deployment led to relative deficits in attention, learning, memory, and reaction-time proficiency.[6]

The pattern of findings was consistent with previous research suggesting that, in the face of threat to one's life, neurobiological alterations in the noradrenergic and neuroendocrine systems[6-10] can result in heightened behavioral reactivity (eg, quickened response times) but dampened attention, learning, and memory for nonthreat-relevant stimuli and events,[9,11,12] allowing cognitive resources to be directed toward survival. While deployed, military personnel often face prolonged exposure to stressful and life-threatening conditions inherent to combat. However, it remains unknown whether deployment-related neuropsychological changes persist over time, are associated with stress-related factors (eg, combat intensity, posttraumatic stress disorder [PTSD] symptoms, and depressive reactions), or are better accounted for by demographic and contextual variables.[7]

This study examined the relative contributions of time since war-zone expo-

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sure, combat intensity, and posttraumatic stress and depression symptoms to postdeployment neuropsychological functioning. Consistent with findings showing that stress-related neurobiological and behavioral alterations in animals and humans may recover over time,[13-15] we hypothesized that, in the absence of additional exposure to combat, longer times since returning from deployment would be associated with greater recovery of neuropsychological functioning (ie, return to baseline). Similarly, we predicted that combat intensity would be associated with neuropsychological functioning among soldiers more recently returned from the war, but not among those who returned from deployment earlier.

Based on previous cross-sectional work indicating greater neuropsychological deficits in trauma survivors with PTSD compared with trauma survivors without PTSD,[16-22] we further predicted that recovery would be moderated by the extent to which soldiers experienced chronic stress-related emotional symptoms (ie, PTSD and depression symptoms). A growing body of work indicates that the nervous system may become progressively overresponsive with time[23-25] and hence associated with increased neural dysregulation (ie, "stress sensitization"),[26-28] leading us to predict that PTSD symptoms would be more strongly related to neuropsychological abnormalities among soldiers assessed at 1-year postdeployment than among soldiers tested recently after their return. With rare exceptions,[29] however, research examining neuropsychological functioning in PTSD has been limited primarily to samples characterized by relatively chronic presentations of PTSD. Little is known about the longitudinal progression of neuropsychological alterations in acute vs chronic PTSD.

METHODS

Human subject approvals were obtained from the human subjects research review boards of the army, Tulane University Health Sciences Center, and the Department of Veterans Affairs. All participants provided written informed consent prior to participation.

STUDY POPULATION AND DESIGN

Two groups of soldiers well matched in military and demographic characteristics were examined across 3 assessments that were temporally linked as closely as possible across the 2 groups (**Figure 1**). Military units in the earlier deployment group were deployed between their baseline (time 1; T1) and interim (time 2; T2) study assessments and were reassessed approximately 1 year after their interim assessments (time 3; T3) following a period of garrison (ie, nondeployed) duty. The recent deployment group did not deploy until after their T2 assessment. Therefore, their T3 assessments were conducted shortly after their return from Iraq. Thus, the labels *earlier* and *recent* pertain not to the actual calendar dates of deployment but rather to the relative recency of return from deployment to the T3 assessment. The staggered timing of the deployments in these 2 groups relative to their longitudinal assessments allowed examination of the influence of time since exposure on neuropsychological outcomes. This report focuses on residualized T3 (postdeployment) outcomes, which take into account baseline function and vary in temporal proximity of return from deployment.

This sample of male and female regular active-duty US Army soldiers serving between April 2003 and August 2006 was drawn from the Neurocognition Deployment Health Study cohort described elsewhere.[30] Although military unit deployment status for each interassessment interval (ie, between T1 and T2, and T2 and T3) could be anticipated by both the participants and examiners, each unit's and each participant's deployment was subject to evolving military operational requirements and was not fully verified until T3. There were 2 subsets of units that comprised the earlier deployment group: those that deployed from November 2003 to November 2004 and those that deployed from late February/early March 2004 to late February/early March 2005. All units comprising the recent deployment group were deployed from November 2004 to November 2005.

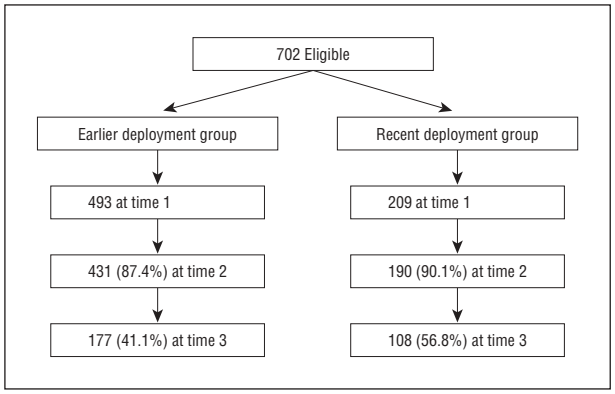

Figure 1. Flowchart of study participants. Values in parentheses depict the percentage of the sample that was retained relative to the previous assessment.

For this study, eligibility criteria included deployment to Iraq during the study period, regular active-duty army status at each of the 3 assessments, freedom from physical limitations that would preclude assessment, and in-person study assessments. The focus on regular active-duty soldiers primarily reflected prioritization of resources to providing information generalizable to the large numbers of military personnel who remain on active duty and may subsequently serve additional war-zone duty.

MEASURES

Comprehensive description of primary assessment data and secondary data obtained from automated military databases is provided elsewhere.[5] Measures relevant to this study follow.

ASSESSMENT PROTOCOL

Demographic, Neuromedical, and Historical Information

Each assessment documented current demographic and military information (eg, age and rank), risk factors for neuropsychological disorders (eg, history of neurodevelopmental disorders, psychiatric disorders, and brain injury), and situational factors (eg, alcohol use) that potentially affect neuropsychological performance. We solicited, by interview, information about all head injuries that resulted in at least momentary loss of consciousness during the study interval. Alcohol use was queried through a paper-and-pencil survey and quantified as the mean number of alcoholic beverages consumed per week during the previous month. Self-reported ethnicity data were gathered to help gauge the representativeness of the sample.

Performance-Based Neuropsychological Tests

Results of a previous factor analysis showed that many of the neuropsychological variables described in previous work[6] represented a single efficiency construct.[31] To avoid multiplicity of outcomes and protect against type I error, analyses included only

Table 1. Subjective Outcomes and Neuropsychological Measures

Instrument	Domain Assessed	Variables	Possible Score Range	Normative/Reference Group Cutoff Score[a,32-40]
Subjective outcome indices				
PCL	Posttraumatic stress symptoms	Summary score	17-85	50[b]
CES-D	Depression symptoms	Summary score	0-27	NA
DRRI combat experiences scale	Combat intensity	Summary score	0-64	NA
Attention, NES3 CPT	Sustained attention/vigilance	No. of omission errors, No. of commission errors (log-transformed)	NA	NA
Learning and memory				
WMS-III, verbal paired associates I	Verbal-auditory learning	Total correct, trials 1-4	0-32	19-21[c]
WMS, visual reproductions II[d]	Visual-spatial memory over time	% Retention	0-100	NA
ANAM simple reaction time	Reaction-time efficiency	Throughput score[e]	NA	218.30 (33.70)[f]

Abbreviations: ANAM, Automated Neuropsychological Assessment Metric; CES-D, Center for Epidemiologic Studies Depression Scale, 9-item version; DRRI, Deployment Risk and Resilience Inventory; NA, not applicable; NES3 CPT, Neurobehavioral Evaluation System, third edition, Continuous Performance Task; PCL, PTSD Checklist; WMS, Wechsler Memory Scale; WMS-III, Wechsler Memory Scale, third edition.

[a] Normative data are not available for the CES-D summary score, log-transformed scores, or scores derived from subtraction and ratio computations.

[b] Positive screening for posttraumatic stress disorder was determined by a score of 50 or higher on the PCL, 1 or more intrusion symptoms, 3 avoidance symptoms, and 2 hyperarousal symptoms of at least moderate severity.

[c] Range that produces a scaled score of 10 for the normative reference group.

[d] Reliability ratings blinded to unit and deployment status performed on 10% of randomly selected drawings indicated high interrater reliability (interrater correlation coefficient, 0.75-0.95).

[e] Throughput scores reflect efficiency (ie, speed in the context of accuracy).

[f] Mean (SD).

outcome measures of theoretical interest (ie, those found to differentiate deployers from nondeployers in the previous report[6]) (**Table 1**). These included residualized T3 values of the Neurobehavioral Evaluation System, third edition,[32] Continuous Performance Task omissions (a sustained attention task requiring detection of targets from distractor stimuli); Automated Neuropsychological Assessment Metric[33] scores (simple reaction-time throughput, a calculated measure of reaction-time efficiency, taking into account accuracy and response time); Wechsler Memory Scale, third edition,[34] verbal paired associates I summary scores (requiring learning of unrelated word pairs); and Wechsler Memory Scale[35] visual reproductions percent retention (requiring reproduction of geometric designs from memory). Percent retention ([delayed recall/immediate recall] × 100) measured memory of visual information over time.

All measures were continuous, reflecting the dimensional nature of the underlying constructs. Continuous measures also increase power for capturing population-based relationships between exposures and performance patterns indicative of brain dysfunction at levels not falling within the range of clinical impairment.

All scores were free of subjective judgment except for visual reproductions, for which designs were scored by a primary rater according to set criteria. Reliability ratings performed on 10% of randomly selected drawings by a second rater blinded to unit and deployment status indicated high interrater reliability (interrater correlation coefficient, 0.75-0.95).

Combat Intensity and Emotional Distress

Combat intensity was quantified by a modified version of the Deployment Risk and Resilience Inventory (DRRI) combat experiences module.[36] Posttraumatic stress disorder and depression symptoms were quantified by the PTSD Checklist (PCL)[37,38] and the Center for Epidemiological Studies Depression Scale, 9-item version (CES-D),[39,40] respectively. All are psychometric self-report inventories yielding continuous variables, with higher scores indicating greater exposure or symptoms.

Assessment of Response Validity

Validity of response profiles on questionnaires was assessed via inspection of scales with bi-directional items (eg, 5 endorses pathologic functioning on some items and intact functioning on others). If a respondent provided all extreme responses in the same direction on a scale with bi-directional items, that respondent's data were not analyzed. Trial 1 of the Test of Memory and Malingering[41] was administered to assess cognitive engagement. The data of participants scoring below 38, a cutoff found to show reasonable sensitivity and specificity in detecting insufficient effort on neurobehavioral tasks,[42] were also excluded from analyses.

ASSESSMENT PROCEDURES

Assessments were conducted at military installations by a civilian examiner team. All performance-based neuropsychological measures were individually administered according to scripted, standardized instructions. Participants completed paper-and-pencil surveys in small groups.

STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS, version 14.0 (SPSS Inc, Chicago, Illinois). When data distributions departed significantly from normal, raw scores were normalized via logarithmic transformation. Missing values for specific items on questionnaires (occurring in <3% of cases) were replaced by the mean value of the individual's completed items for that measure if the participant responded to at least 50% of the items. If less than 50% of the items on a measure were completed, summary scores were not computed. Outliers were truncated at 3 standard deviations (SDs) from the mean.

Differences in both baseline (T1) and interim (T2) characteristics between T3 participants and nonparticipants were examined via 2-tailed t or χ^2 tests, as appropriate, to provide a comprehensive analysis of potential response bias. Differences between earlier and recent deployment groups in interassessment interval duration were compared using 2-tailed t tests. To determine the relationship between interval durations and performance, we conducted partial correlations within each group and within the overall sample between interval duration and each of the T3 neuropsychological outcome measures controlling for core covariates (T1 age, T1 education, T3 alcohol use, head injury between T1 and T3, and T1 neuropsychological performance). Differences in baseline character-

istics and predictor variables (T3 PCL and CES-D scores, DRRI combat experiences scores, and T1-T3 and deployment head injury) between earlier and recent deployment groups were compared with unadjusted 2-tailed t and χ^2 tests, as appropriate. Group differences in change in neuropsychological performances over the deployment interval and from T1 to T3 for each group were examined via 2-tailed t tests, with performance scores adjusted for T1 age, T1 education, time-specific alcohol use, and head injury between T1 and T3.

Multiple regression analyses examined adjusted associations between T3 neuropsychological performances and time since deployment (dummy coded as recent vs earlier), T3 PCL and CES-D summary scores, and DRRI combat experiences summary scores. Covariates included T1 levels of neuropsychological performance and demographic and contextual variables potentially related to outcomes (T1 age and education, brain injury during the study period, and T3 alcohol consumption). Interaction terms were created to examine whether time since deployment modified the relationship of neuropsychological outcomes with PTSD symptoms, depression symptoms, and combat intensity.

Because we examined only 4 outcome variables, each of which measured a unique construct, significance levels were set at 2-tailed $P < .05$ with no further adjustment. Power analysis indicated 80% power to detect an effect size of 0.35 at the 2-tailed .05 α level for unadjusted comparison of means between 164 earlier deployed and 104 recently deployed soldiers. For multiple regression analyses, assuming 5 to 10 covariates in the model that explain at least 10% of the variability in outcome, we had 80% power of detecting an association corresponding to an increase in R^2 of 0.025.

RESULTS

SAMPLE DERIVATION AND CHARACTERISTICS

Of the 621 potentially eligible regular active-duty participants who underwent testing at T1 and T2, 285 (46%) participated in person at the T3 assessment (Figure 1). The predominant reason for T3 nonparticipation was relocation to another military installation (**Table 2**). Such relocation reflects the 3-year rotation schedules that characterized the army during the study period. Of the 285 T3 participants, 12 were excluded because of missing data, 3 for invalid questionnaires or questionable cognitive effort, and 2 because they did not deploy, resulting in a final sample of 268 (164 earlier deployers and104 recent deployers). All but 12 participants served full 12-month overseas rotations.

Participants in the final sample generally reflected the broader Operation Iraqi Freedom–deployed army population (**Table 3**). Women were slightly underrepresented. Although enlisted personnel constitute the majority of deployers, commissioned officers were also underrepresented. Less than 2% of participants had previously been deployed to Iraq or Afghanistan. At T3, participants reported consuming 7.27 (SD, 9.85) alcoholic beverages per week. Twenty-seven (approximately 10%) reported sustaining a brain injury during deployment, most of which were mild. Of these 27 soldiers reporting brain injury, 13 (48%) reported loss of consciousness of less than a minute and only 6 (22%) reported trouble remembering the injury event.

Table 2. Reasons for Nonparticipation Among Those Remaining in Military Service at Time 3[a]

Reason for Nonparticipation	Participants, No. (%)	
	Earlier Deployment	Recent Deployment
Time 1 to Time 2		
No. of participants	62	19
Reassignment to another military unit	30 (48.4)	14 (73.7)
On leave/at training/on special assignment	23 (38.0)	2 (10.5)
Declined	7 (11.3)	1 (0.5)
Deployed at time 2	NA	1 (0.5)
Sick/injured	1 (1.6)	0
Unknown[b]	1 (1.6)	1 (0.5)
Time 2 to Time 3		
No. of participants	254	82
Reassignment to another military unit	227 (89.4)	53 (64.6)
On leave/at training/on special assignment	15 (5.9)	24 (29.3)
Declined	6 (2.4)	2 (2.4)
Sick/injured	5 (2.0)	2 (2.4)
Unknown[b]	1 (0.4)	1 (0.1)

Abbreviation: NA, not applicable.
[a] Time 1, baseline; time 2, interim; time 3, postdeployment (proximal to return for recent deployers; 1 year following return for earlier deployers).
[b] Includes soldiers who were reportedly no longer with their unit but for whom military administrative records were not accessible for verification of reassignment or separation from service.

EARLIER VS RECENT DEPLOYERS

Groups did not differ in T1 military characteristics, demographics, or extent of neuropsychological change displayed from predeployment to postdeployment (Table 3 and **Table 4**). However, they differed in the percentage of individuals reporting sustaining a head injury with loss of consciousness during the study period.

T3 PARTICIPANTS VS NONPARTICIPANTS

Within the earlier deployment group, there were no differences between participants and nonparticipants on demographic variables, T1 and T2 neuropsychological outcomes, T1 and T2 PCL scores, T1 and T2 head injury, T2 CES-D scores, or DRRI combat experiences scores. Within the recent deployment group, participants were younger ($P = .002$), had fewer years of education ($P = .02$), and displayed less proficient T2 visual memory than nonparticipants ($P = .03$) but did not differ on any of the T1 or T2 neuropsychological outcomes. Recent deployment participants also reported less T1 (but not T2) head injury ($P = .02$) than recent deployment nonparticipants.

ASSESSMENT INTERVALS

For earlier deployment soldiers, T1 assessment was conducted 78.74 days (SD, 82.41 days; median, 42 days) before deployment; T2 assessments were conducted 72.34 days (SD, 14.91 days; median, 77 days) after return from Iraq for those serving full tours; T3 assessments were conducted 449.45 days (SD, 65.10 days; median, 404 days)

Table 3. Demographic and Contextual Sample Characteristics at Baseline[a]

Variable	No. (%)		
	Overall Sample (N=268)	Earlier Deployment (n=164)	Recent Deployment (n=104)
Age, mean (SD), y	24.47 (4.83)	24.33 (4.77)	24.70 (4.93)
Race/ethnicity			
White	147 (55.1)	84 (51.2)	63 (61.2)
African American	39 (14.6)	26 (15.9)	13 (12.6)
Hispanic American	38 (14.2)	28 (17.1)	10 (9.7)
Asian American	15 (5.6)	6 (3.7)	9 (8.7)
Other	28 (10.5)	20 (12.2)	8 (7.8)
Female sex	18 (6.7)	11 (6.7)	7 (6.7)
Education, mean (SD), y	12.38 (1.20)	12.32 (1.03)	12.48 (1.41)
Time in army, mean (SD), y	3.71 (3.76)	3.67 (3.80)	3.77 (3.71)
Rank, enlisted			
Junior enlisted, E1-E4	204 (76.1)	126 (76.8)	78 (75.0)
Noncommissioned officers, E5-E9	59 (22.0)	37 (22.6)	22 (21.2)
Officers, commissioned or warrant	5 (1.9)	1 (0.6)	4 (3.8)
Previous operational deployment	26 (10.1)	15 (9.1)	11 (11.8)
Married	121 (45.1)	75 (45.7)	46 (44.2)
Amount of sleep/night in past week, mean (SD), h	5.99 (1.32)	5.91 (1.37)	6.11 (1.22)
Alcoholic drinks consumed/wk in past month, mean (SD)	8.34 (12.34)	8.24 (12.34)	8.49 (12.40)
Current cigarette smoker	133 (49.6)	83 (50.6)	50 (48.1)
Reported taking prescribed or OTC medication in the past 48 h	77 (28.7)	45 (27.4)	32 (30.8)
Reported taking prescribed psychoactive or anticonvulsant medications in the past 48 h	4 (1.5)	2 (1.2)	2 (1.9)
Reported developmental disorder	31 (11.6)	15 (9.1)	16 (15.5)
Reported psychiatric disorder	13 (4.9)	7 (4.3)	6 (5.8)
Reported past alcohol use disorder	16 (6.0)	11 (6.7)	5 (4.8)
Reported other neuromedical disorder	5 (1.9)	5 (3.2)	0

Abbreviations: E, enlisted; OTC, over-the-counter.
[a]The sample size varies slightly across observations owing to missing data.

Table 4. Comparison of Stress Response, Head Injury, and Neuropsychological Scores

Variable	Mean (SD)		*P* Value
	Earlier Deployment	Recent Deployment	
Stress response measures			
PCL T1, summary score	28.51 (11.77)	28.00 (11.44)	.73
PCL T3, summary score	29.23 (12.19)	29.64 (12.02)	.79
CES-D T3, summary score	6.94 (5.00)	6.48 (4.64)	.46
DRRI combat experiences, summary score[a]	18.96 (10.39)	19.22 (10.21)	.85
Self-reported head injury with loss of consciousness, No. (%)			
During deployment	12 (7.3)	15 (14.4)	.06
T1-T3	14 (8.5)	20 (18.4)	.02
Neuropsychological difference scores over deployment[b]			
NES3 CPT, log-transformed omission errors	0.04 (0.53)	0.19 (0.55)	.30
WMS-III VPA, learning trials, No. correct	1.61 (6.84)	0.52 (6.13)	.38
WMS visual reproductions, % retention	–2.86 (20.51)	–0.38 (21.40)	.09
ANAM simple reaction-time throughput	–0.12 (32.99)	8.98 (28.71)	.83

Abbreviations: ANAM, Automated Neuropsychological Assessment Metric; CES-D, Center for Epidemiologic Studies Depression Scale; DRRI, Deployment Risk and Resilience Inventory; NES3 CPT, Neurobehavioral Evaluation System, third edition, Continuous Performance Test; PCL, PTSD Checklist; T1, time 1 (baseline); T2, time 2 (interim); T3, time 3 (postdeployment [proximal to return for recent deployers; 1 year following return for earlier deployers]); WMS, Wechsler Memory Scale; WMS-III VPA, Wechsler Memory Scale, third edition, verbal paired associates.
[a]Time 2 for earlier deployment is compared with T3 for recent deployment.
[b]For earlier deployment, T2 minus T1; for recent deployment, T3 minus T2.

after return from Iraq for those serving full tours. For recent deployment soldiers, T1 assessments were conducted 378.12 days (SD, 15.0 days; median, 378 days) before deployment; T2 assessments were conducted 157.73 days (SD, 62.28 days; median, 175 days) before deployment; T3 assessments were conducted 122.98 days (SD, 8.04 days; median, 122 days) after return for those serving full tours. The mean duration of T1/T3 interassessment intervals for earlier and recent deployment participants was 885.07 days (SD, 142.09 days; median, 791 days) and 854.39 days (SD, 1.98 days; median, 855 days), respectively ($t=-2.24$, $P=.005$). Of 12 possible correlations (4 outcomes × 3 groupings: recent deployed, earlier deployed, and overall sample) between assessment interval and the neuropsychological outcomes, none reached statistical significance (all $P>.05$; range, $P=.06$-$.93$).

ASSOCIATIONS WITH TIME SINCE DEPLOYMENT, COMBAT INTENSITY, AND PSYCHIATRIC SYMPTOMS

Baseline and T3 postdeployment means and SDs for outcome measures and frequencies of participants in each group exceeding deficit cut-off scores are presented in **Table 5**. The 2 groups did not differ significantly in change from T1 to T3 on any of the neuropsychological performance measures ($P>.05$; range, $P=.09$-$.83$).

Demographic and contextual factors (head injury and alcohol consumption) were not associated with residualized T3 neuropsychological outcomes. There was a positive association between educational attainment and visual reproduction, percent retention (B=1.67, $P=.04$), in which higher educational attainment was associated with greater performance proficiency. No other covariates were significantly related to T3 outcomes in the final models.

After taking into account variance attributable to covariates, results revealed that time since deployment was not significantly related to neuropsychological performance in the overall sample (**Table 6**). However, among participants with higher levels of PTSD symptoms, time since deployment was related to attention performance (unstandardized B for interaction=–0.01, $P=.04$). Greater PTSD symptoms were significantly related to poorer attention in soldiers who were tested at 1-year follow-up

Table 5. Scores on Primary Outcome Measures at Predeployment and Postdeployment Among Earlier Deployers and Recent Deployers[a]

	Mean (SD)			
	Predeployment		Postdeployment	
Outcome Variable	Earlier Deployment	Recent Deployment	Earlier Deployment	Recent Deployment
NES3 CPT, omission errors[b]	0.29 (0.50)	0.23 (0.44)	0.31 (0.53)	0.32 (0.55)
WMS-III verbal paired associates, learning trials, No. correct	17.69 (7.18)	17.63 (7.15)	22.77 (6.44)	21.71 (7.10)
WMS visual reproduction, % retention	90.88 (12.21)	92.50 (10.99)	90.62 (12.68)	87.55 (18.21)
ANAM simple reaction-time throughput	183.51 (28.45)	184.59 (29.32)	185.79 (27.02)	187.84 (27.55)

Abbreviations: ANAM, Automated Neuropsychological Assessment Metric; NES3 CPT, Neurobehavioral Evaluation System, third edition, Continuous Performance Test; WMS, Wechsler Memory Scale; WMS-III, Wechsler Memory Scale, third edition.
[a] Postdeployment reflects 1-year follow-up for the earlier group and recent postdeployment for the recent group.
[b] Log-transformed. Lower scores reflect better functioning for NES3 CPT. Higher scores reflect better functioning on verbal paired associates, visual reproductions, and simple reaction-time tasks.

Table 6. Regression Results for the Effects of Time 3 PCL and CES-D Scores, DRRI Combat Experiences Score, and Time Since Deployment on Time 3 Neuropsychological Performance[a]

	NES3 CPT, Omission Errors[b]		WMS-III Verbal Paired Associates, Learning Trials, No. Correct		WMS Visual Reproductions, % Retention		ANAM Simple Reaction-Time Throughput	
Variable	B (95% CI)	*P* Value	B (95% CI)	*P* Value	B (95% CI)	*P* Value	B (95% CI)	*P* Value
PCL summary score	0.01 (0.00 to 0.02)	.11	0.03 (–0.05 to 0.11)	.47	0.00 (–0.23 to 0.22)	.97	–0.24 (–0.63 to 0.16)	.24
CES-D summary score	0.00 (–0.02 to 0.02)	.80	0.02 (–0.19 to 0.22)	.88	–0.20 (–0.74 to 0.35)	.48	–0.17 (–1.13 to 0.78)	.72
DRRI combat experiences summary score	0.00 (–0.01 to 0.01)	.92	0.01 (–0.06 to 0.08)	.85	–0.02 (–0.20 to 0.17)	.85	0.48 (0.16 to 0.81)	.004
Deployment time, recent vs earlier	0.03 (–0.11 to 0.16)	.68	–0.95 (–2.31 to 0.41)	.17	–3.43 (–7.13 to 0.28)	.07	1.42 (–5.05 to 7.89)	.67
PCL × deployment time	–0.01 (–0.02 to 0.00)	.04	0.03 (–0.08 to 0.15)	.59	–0.07 (–0.38 to 0.24)	.66	0.18 (–0.36 to 0.72)	.51
CES-D × deployment time	–0.02 (–0.05 to 0.01)	.15	–0.12 (–0.41 to 0.16)	.40	–0.32 (–1.10 to 0.45)	.41	–0.78 (–2.14 to 0.58)	.26
DRRI × deployment time	0.00 (–0.01 to 0.01)	.89	0.07 (–0.07 to 0.20)	.33	–0.09 (–0.44 to 0.27)	.64	–0.03 (–0.66 to 0.61)	.94

Abbreviations: ANAM, Automated Neuropsychological Assessment Metric; CES-D, Center for Epidemiological Studies Depression Inventory; CI, confidence interval; DRRI, Deployment Risk and Resilience Inventory; NES3 CPT, Neurobehavioral Evaluation System, third edition, Continuous Performance Test; PCL, PTSD Checklist; WMS, Wechsler Memory Scale; WMS-III, Wechsler Memory Scale, third edition.
[a] Model core covariates are time 1 (baseline) values of neuropsychological performance and demographic/contextual variables potentially related to outcomes (time 1 age and education, brain injury during the study period, and time 3 alcohol consumption). Time 3 indicates postdeployment (proximal to return for recent deployers; 1 year following return for earlier deployers).
[b] Log-transformed.

(B=0.01, *P*=.03) but not for participants who had recently returned (B=0.00, *P*=.84) (**Figure 2**). At 1-year follow-up, mean adjusted log-transformed attention error scores increased by 0.10 points for every 10 points on the PCL. Higher levels of combat exposure were associated with more efficient postdeployment reaction-time performances, regardless of time since deployment (B=0.48, *P*=.004) (**Figure 3**), with mean adjusted reaction efficiency scores increasing by 4.8 points for every 10 points on the combat experiences scale.

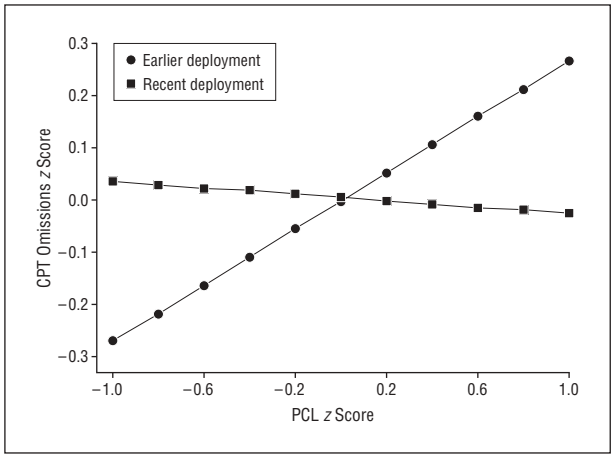

Figure 2. Relationship of PTSD Checklist (PCL) summary *z* scores to log-transformed Continuous Performance Test (CPT) omission *z* scores among recent and earlier deployers.

COMMENT

At T3, the only variable associated with an adverse neuropsychological outcome was PTSD symptom severity among soldiers who had been back from Iraq for a year. Neuropsychological performance at T3, adjusted for predeployment levels, was not related to time since return

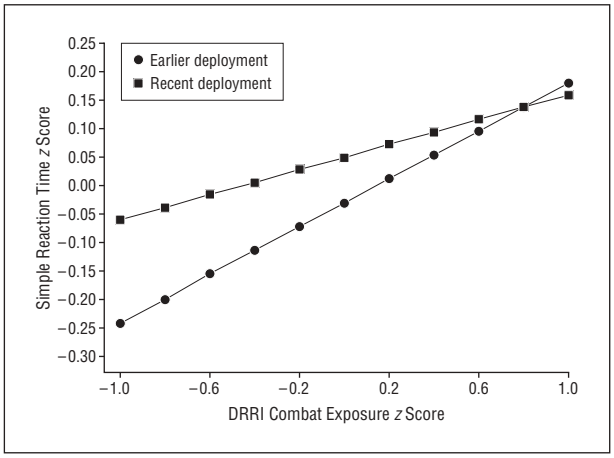

Figure 3. Relationship of Deployment Risk and Resilience (DRRI) combat experiences summary *z* scores to simple reaction-time throughput *z* scores among recent and earlier deployers.

from deployment independent of PTSD symptom severity. Thus, in the absence of PTSD, neuropsychological functioning appears to remain stable for more than 1 year after return from deployment.

Higher levels of combat intensity during deployment were associated with more efficient reaction-time responses, regardless of time since deployment. Thus, whereas higher levels of PTSD symptoms were associated with less proficient performance on a neuropsychological task (attention) at 1-year follow-up, higher levels of combat intensity were associated with enhanced neuropsychological performance on a reaction-time test among both soldiers tested immediately after return and among those who had been back from war for a year. The significant relationship between combat intensity and reaction-time efficiency is consistent with previous findings[6] and suggests that the previously observed relationship between deployment and reaction time may have been attributable to deployment-related combat exposure. Results also suggest that combat intensity has both acute and lasting associations with reaction time. In the current context of multiple deployments, active-duty soldiers complete intensive training and preparations between deployments. Thus, if reaction time represents enhanced cognitive "readiness," the seemingly prolonged association of prior combat experience with behavioral reactivity may instead reflect an adaptive preparatory response associated with upcoming war-zone deployment.

The interaction between time since return from deployment and PTSD symptoms suggests that chronic PTSD symptoms are associated with attentional impairment for emotionally neutral information. The specificity of the decrement in attention to PTSD symptoms, but not depression, bolsters research documenting cross-sectional relationships between PTSD and neuropsychological functioning.[16,17,21,43,44] Thus, from a neuropsychological perspective, PTSD symptoms and their neurobiological substrates appear more important than other stress-related (eg, depression) or exposure (eg, head injury and combat exposure) variables in predicting adverse neuropsychological outcomes in soldiers a year after their return from deployment.

These results also have implications for the natural progression of PTSD symptoms. Specifically, when viewed in concert with the association between reaction time and combat exposure in both soldiers who had recently returned and those returning a year prior, the results suggest that relatively acute PTSD symptoms may exert less of an effect on attention than more chronic PTSD symptoms. Such a pattern would be consistent with a stress sensitization model of PTSD,[26-28] which purports that stress exposure leads to changes in neurotransmitter and neurohormonal response that, in some cases, generate or exacerbate PTSD symptoms. The PTSD symptoms, in turn, further promote increased overreactivity of the nervous system.

It may also be that the association between PTSD symptoms and attentional impairment at T3 represented a preparatory response in anticipation of a subsequent war-zone deployment. Many of the soldiers in this cohort would have been anticipating at least the possibility, if not the certainty, of an upcoming deployment. Reduced proficiency on an emotionally neutral task of sustained attention is consistent with research demonstrating that PTSD is associated with the tendency to direct attention toward emotionally relevant information (in this case, upcoming war-zone deployment) at the expense of attention to emotionally neutral stimuli (in this case, a neutral attentional task).[45-47] Such PTSD-related attentional biases are thought to represent perpetuations of formerly adaptive survival responses to threat and are not mutually exclusive with stress sensitization.

Our finding indicating that the relationship between PTSD and attentional impairment is minimal early on but strengthens over time is consistent with previous research. For example, Brandes et al[48] found no significant relationship between PTSD and neuropsychological performance within 10 days of trauma exposure. Bustamante et al[49] reported longitudinal findings similar to ours, albeit within an abbreviated time frame. Shortly after trauma exposure, PTSD was not significantly related to neuropsychological performance; however, over time, PTSD symptoms negatively correlated with neuropsychological performance. Importantly, the results of our study and previous research suggest that PTSD-related attentional impairments are mild compared with those expressed in overt neurological disorders, such as degenerative dementia or cerebrovascular disease. Nevertheless, the deficits represent changes relative to the soldier's previous functioning that are potentially distressing, especially if exacerbated over time as PTSD symptoms become even more chronic.

The lack of a significant association between neural risk factors (ie, head injury with loss of consciousness and recent alcohol consumption) and neuropsychological outcomes is somewhat surprising, as both traumatic brain injury and alcohol toxicity are associated with neuropsychological compromise.[50-52] However, the low prevalence of self-reported head injury and restricted range of alcohol use in this sample may not have allowed detection of relationships between these factors and neuropsychological outcomes.

Recent findings reveal notably high rates of poor mental health outcomes among US service members upon return from Iraq deployment.[5,53-55] Our findings additionally highlight the neuropsychological consequences of

chronic PTSD symptoms. Although neuropsychological changes were not profound and, for reaction time, can be construed as desirable in the short-term, their significance lies in the demonstration that psychiatric symptoms often reflect more extensive biological changes, including those affecting brain functioning. A growing literature demonstrates the significant impact of prolonged and repetitive stress on health factors (eg, immune functioning,[56] cardiovascular disease,[57] and other systemic medical illnesses[58-60]) that can be traced to the biological stress response.[8,11] Thus, subtle cognitive changes (positive or negative) associated with combat exposure or PTSD may represent a warning sign relevant to long-term health.

Study findings may not generalize to other military branches or to service members not remaining in the military after war-zone service. Our relatively low longitudinal retention also potentially limits the generalization of results. However, loss to follow-up was largely attributable to the standard rotational reassignment of soldiers to different military installations. Consistent with recent findings among British Iraq War veterans,[61] we found few differences between participants and nonparticipants on key outcomes measured in previous assessments, suggesting no systematic relationship between outcomes and likelihood of T3 participation. A nondeployed comparison group followed up for the longitudinal duration of the study would have allowed firmer conclusions regarding the natural course of functioning. However, the current pace of deployment dictates that military personnel comparable in training with deployed personnel inevitably deploy, rendering identification of an appropriate comparison group over the entire duration of a multi-year longitudinal study highly unlikely. Despite these limitations, the longitudinal design, objective neuropsychological measures, and a comparison sample well matched in military and demographic characteristics provide unique information regarding the longitudinal trajectory of objectively measured neuropsychological alterations associated with deployment and their relationship to war-zone stress.

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