

# Factors influencing cognitive functioning following mild traumatic brain injury in OIF/OEF burn patients<sup>1</sup>

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**Abstract.** *Objective:* To examine the relationship between mild traumatic brain injury (mTBI), psychiatric conditions, pain medications, and injury severity on cognitive functioning in service members admitted to a burn unit. We hypothesize that psychiatric co-morbidity and pain medications will have a stronger relationship with cognitive dysfunction than mTBI diagnosis in this population.

*Method:* Retrospective review of clinical evaluations ( $n = 194$ ) completed between September 2005 – October 2007 on service members with burn injuries secondary to explosive munitions. Evaluations were completed during the acute stage of recovery (mean = 7.87 weeks). mTBI diagnosis ( $n = 50$ ) was made through a clinical interview using ACRM criteria [1]. Exclusion criteria included duration of posttraumatic amnesia > 24 hours ( $n = 10$ ); and inability to complete neurocognitive measures due to severe bimanual burns and/or amputations ( $n = 17$ ). Cognitive functioning was evaluated using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).

*Results:* Subjects who sustained mTBI demonstrated significantly greater difficulty on the RBANS visuospatial and attention/processing speed indices. A hierarchical linear regression, using mTBI diagnosis, psychiatric diagnosis, time since injury, presence of pain medications, and measures of trauma severity as predictive factors, found that mTBI diagnosis had a significant, but small unique effect on cognitive functioning. Contrary to our hypothesis, psychiatric co-morbidity was not shown to have a significant effect on this population of acutely injured service members.

*Conclusions:* While the relationship between severe TBI and cognitive functioning is well established, the relationship between mTBI and its effects on cognitive and behavioral abilities is less clear. The current study demonstrates that mTBI and analgesic medications have a small effect neurocognitive functioning in this population. Continued examination of this relationship is warranted.

**Keywords:** Mild traumatic brain injury, blast injury, cognitive dysfunction

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## 1. Introduction

Considerable focus has been placed upon the identification and treatment of traumatic brain injury (TBI) in service members returning from combat-deployment [26]. Several recent studies provide incidence estimates for mild TBI among combat deployed troops serving in OIF/OEF. In one cross-sectional study of OIF/OEF service members, 12% of the population of over 2,200 respondents to a mail survey reported a history consistent with mild TBI during deployment [24]. In another recent study, 4.9% of over 2,500 Army infantry soldiers reported mild TBI with loss of consciousness and another 10.3% reported mild TBI with altered mental status [11]. These relatively high rates of mild brain injury in current military conflicts reflect the specific nature of the conflict, in particular the frequent use of explosive munitions, as well as reduced mortality from improvements in body armor and greater knowledge and awareness of mild TBI arising from civilian and sports-related injuries.

A common cause of combat injury in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) is explosive munitions. It has been reported that approximately two-thirds of OIF/OEF Army evacuations from combat theater prior to 2006 were related to blast explosions [26]. In contrast to general population-based statistics, the incidence of mTBI in OIF/OEF trauma patients exposed to explosive munitions (59%) is quite high [10]. Little is known about the cognitive sequelae of this population, or its relationship to trauma severity, co-existing conditions, and medications.

Cognitive complaints such as distractibility, attention deficits, poor working memory and inefficient mental processing are commonly associated with mild TBI. The mild TBI literature in civilians suggests that symptomatic recovery from mild TBI typically occurs within 3 months post injury. Postconcussive syndrome (PCS) is often diagnosed when symptoms persists beyond six months [6]. Equivalent outcomes have resulted when comparing PCS based on DSM-IV criteria to diagnosis by ICD-10 [17]. However, it is also well-established that cognitive symptoms are not specific to mild TBI, occurring in other conditions [15] as well as in the normal population [14]; and are influenced by gender, pain, psychiatric history [19] and other psychosocial and environmental factors [8]. Of particular relevance to symptom report after injury in the deployed setting is the occurrence of posttraumatic stress. It is well-acknowledged that there is significant symptomatic overlap between postconcussive and posttraumatic

stress-related symptoms, including alterations in cognitive function [11,24]. As stated recently by Powell [21], the importance of considering base rates of postconcussive symptoms in non-TBI populations is crucial to making correct diagnostic attributions.

Neuropsychological testing is useful for evaluating cognitive status and providing objective information to supplement symptom report. In the acute post-TBI period neuropsychological test results are able to discriminate patients with mild TBI from other medical patients, whereas cognitive symptom complaints generally do not [13,14]. In recognition of the value of early cognitive assessment, neuropsychological evaluation of cognitive function is a standard following sports-related concussion [16,20].

The current research on the impact of mTBI on cognitive functioning among blast-injured soldiers has been limited. The primary aim of this study is to examine the relationship between cognitive functioning and potential influencing factors including trauma severity, psychiatric conditions, mTBI, and analgesic pain medications. A secondary aim was to examine neurocognitive performance in service members who sustained mTBI in comparison to those who were injured in blasts but did not sustain mTBI. We hypothesize that psychiatric co-morbidity; particularly PTSD, will have a stronger relationship to cognitive dysfunction than mTBI diagnosis in this population. We also hypothesize that cognitive dysfunction will be related to pain medication use in acute trauma patients. Participants included consecutive admissions of OIF/OEF military service members from September 2005 through October 2007 to the burn ward at Brooke Army Medical Center (BAMC). This strategy avoided the methodological bias inherent in using a selected sample, such as patients referred for cognitive evaluations due to symptom complaints.

## 2. Methods

### 2.1. Participants

The sample consisted of 194 US military service members with burn injuries due to explosive munitions treated at BAMC between September 2005 and October 2007. Service members who sustained a blast injury were referred to the Neuropsychology Service as part of routine screening for clinical evaluation and neurocognitive testing. All subjects included in this study were at

Table 1  
Demographic information

|           | TBI+<br><i>n</i> = 50 | TBI-<br><i>n</i> = 117 | <i>p</i> value |
|-----------|-----------------------|------------------------|----------------|
| Age       | 25.06 (5.818)         | 25.67 (5.537)          | 0.524          |
| Education | 12.54 (1.073)         | 12.52 (1.454)          | 0.935          |
| Gender    | 44 (88.0%) male       | 114 (97.4%) male       | 0.013          |

Note: values are mean and (SD).

least 18 years of age, spoke English, and had sustained an injury while on active duty military service.

Mild TBI was defined as loss of consciousness (< 30 minutes); loss of memory for events immediately before (retrograde amnesia) or after the accident (post traumatic amnesia (PTA) < 24 hours); any alteration in mental state at the time of the injury (dazed, disoriented, confused); and a Glasgow Coma Scale score  $\geq$  13, if available [1]. Presence and severity of TBI was determined from detailed clinical interviews and review of records conducted by two clinical neuropsychologists at Brooke Army Medical Center.

Ten participants were excluded due to a duration of PTA > 24 hours, suggesting a more severe brain injury than ACRM criteria. Additionally, 17 subjects were excluded because they could not complete the manual portion of neuropsychological testing due to severe bilateral burns and/or amputations. Although patients were screened for a pre-existing neurological disorder, no subjects met this exclusion criterion. Participants were not excluded based on a co-morbid psychiatric disorder or history of psychiatric disorder or condition. Psychiatric diagnosis was made through semi-structured clinical interview, documented in the medical record at the time of neuropsychological evaluation. Clinical examination reflected a broad range of diagnoses (e.g., Adjustment Disorder; Acute Stress Disorder; Major Depressive Disorder), oftentimes with overlapping symptomatology. As a result, psychiatric diagnosis was coded for the presence or absence of any co-morbid psychiatric condition for the purpose of this study. Similarly, narcotic pain medications were dichotomized (i.e., presence or absence), as the systemic levels of narcotic medications could not be obtained.

Demographic variables and injury characteristics are summarized in Tables 1 and 2. The study population was divided into two groups on the basis of mTBI diagnosis, resulting in mTBI positive (*n* = 50) and mTBI negative (*n* = 117) subgroups for comparison.

## 2.2. Measures and procedures

TBSA and ISS were calculated by medical personnel on the BAMC burn unit at the time of admission.

TBSA is a standardized classification system utilized to approximate the amount of body area covered by burns [2]. The Injury Severity Score (ISS) is an anatomical scoring system which provides a quantifiable score based on the location, survivability, and number of injuries. This score ranges from 0 to 75 and is correlated with mortality, morbidity and length of hospital stay [3].

After being determined medically stable, patients were administered the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). The RBANS is a widely used measure of cognitive functioning and provides five domain index scores and a combined total index score. The domain specific indexes are Immediate Memory, Visuospatial/Constructional, Language, Attention, and Delayed Memory [22,23]. The RBANS has been validated to assess cognitive functioning among a variety of populations including traumatic brain injury [18], dementia [9], stroke [27], schizophrenia [28], substance abuse [25] and multiple sclerosis [4].

## 2.3. Statistical analyses

First, to protect against experiment-wise error, an analysis of variance (ANOVA) for the RBANS Total Score was used to compare the TBI and non-TBI groups. If significant, additional ANOVAs for each RBANS subscale were planned. Hierarchical linear regression analyses were then used to examine the relationship between cognitive functioning and possible predictor variables: demographic characteristics (age, education, and race), trauma characteristics (TBSA, ISS, and time post-injury), psychiatric conditions, mTBI, and analgesic pain medications. Continuous independent variables were: age, education, weeks post-injury, TBSA, and ISS. Dichotomous independent variables were: race (majority/minority), mTBI diagnosis; psychiatric diagnosis; and presence of narcotic medications. The interaction between TBI and psychiatric diagnosis was also examined. Variables were entered in blocks, with the main effects entered first followed by the interaction. To determine the unique contribution of each set of predictor variables, each block was entered last relative to all other blocks of predictors. The change in variance associated with the last step represents the unique contribution of that set of predictors. This procedure was used to evaluate the unique contribution of the main effects prior to the interaction effects, as well as the unique contribution of the interac-

Table 2  
Injury-related variables

|                        | TBI+<br><i>n</i> = 50 | TBI–<br><i>n</i> = 117 | <i>p</i> value |
|------------------------|-----------------------|------------------------|----------------|
| Weeks Post Injury      | 8.12 (7.763)          | 7.76 (8.181)           | 0.792          |
| TBSA                   | 12.70 (11.171)        | 15.87 (16.625)         | 0.220          |
| ISS                    | 11.48 (10.031)        | 12.25 (11.765)         | 0.687          |
| Psychiatric Diagnosis+ | 25 (50.0%)            | 26 (22.2%)             | 0.001          |
| Pain Medication+       | 32 (64.0%)            | 85 (72.6%)             | 0.264          |

Note: values are mean and (SD).

Table 3  
Cognitive performance by domains

|                             | TBI+<br><i>n</i> = 50 | TBI–<br><i>n</i> = 117 | <i>p</i> value |
|-----------------------------|-----------------------|------------------------|----------------|
| Immediate Memory            | 95.14 (14.181)        | 96.49 (14.445)         | 0.589          |
| Delayed Memory              | 96.48 (12.998)        | 100.42 (12.854)        | 0.072          |
| Visuospatial/Constructional | 104.06 (13.382)       | 109.29 (10.470)        | 0.007          |
| Language                    | 92.90 (15.586)        | 93.66 (11.873)         | 0.732          |
| Attention                   | 84.06 (15.013)        | 89.74 (14.898)         | 0.026          |
| Total                       | 92.16 (11.932)        | 96.71 (11.672)         | 0.023          |

Table 4  
Variance in RBANS attention/processing speed index explained by predictor variables

| Variables                            | Unique variance | Total variance |
|--------------------------------------|-----------------|----------------|
| Demographic                          | 4.8%            |                |
| Injury Characteristics               | 2.3%            |                |
| TBI Diagnosis                        | 3.6%            |                |
| Psychiatric Diagnosis                | 0.1%            |                |
| Pain Medication                      | 1.6%            |                |
| Interaction of TBI and Psychiatric   | 0.1%            |                |
| Total Variance Prior to Interaction  | 12.5%           | 12.8%          |
| Total Variance Including Interaction | n.a.            | 12.9%          |
| Shared Variance Among Predictors     | n.a.            | 0.4%           |

tion between TBI and comorbid psychiatric conditions over and above the main effects.

Given that the RBANS Attention/Processing Speed Index has been demonstrated to be the most sensitive measure of cognitive dysfunction in this instrument following traumatic brain injury [22], this score was chosen as the dependent variable.

### 3. Results

The RBANS scores are interval data with a normative mean of 100 and a standard deviation of 15. An analysis of variance comparing the groups (TBI+, TBI–) on the RBANS Total Score was significant (see Table 3). Post hoc analyses of the RBANS subtests revealed that the TBI Positive group scored significantly lower ( $\alpha = 0.05$ ) than the TBI Negative group on two of the Cognitive Performance Domains, i.e., the Visuospatial/Constructional Domain and the Attention Domain

(see Table 3). The group differences were small and not clinically significant and overall scores were in the average range, apart from the Attention subscale.

The previously described hierarchical logistic regression procedure was used to determine which factors associated with RBANS Attention/Processing Speed Index. The overall model was significant, but only accounted for 12.9% of the total variance in Attention/Processing Speed Index [ $F(10, 156) = 2.31, p < 0.02$ ]. As seen in Table 4, the largest predictors in the model were demographic factors (4.9%), followed by TBI (3.6%), and injury variables (2.3%), all of which were statistically significant. Neither pain medication (1.6% of variance) nor psychiatric diagnosis (0.1%) accounted for a significant amount of variance in the Attention/Processing Speed Index.

These results indicate that blast-injured burn subjects in the acute recovery phase are likely to perform slightly worse on measures of attention and processing speed if they sustained a mild TBI. In contrast, psychiatric co-

morbidity was not demonstrated to have a statistically significant effect on cognitive functioning.

#### 4. Discussion

In the acute phase of recovery following burn trauma, the presence of mTBI was associated with slightly lower performance on cognitive measures, particularly attention/speed of processing. This finding is consistent with prior studies suggesting that small changes on objective neuropsychological measures can be observed in the acute phase of recovery following mTBI [13,14], as well as in blast-injured service members [5]. As expected given the milder severity of injury, the burn trauma patients in this population performed dramatically better than the severely brain injured subjects in other published studies of RBANS performance [18,22]. It is important to note that the mean cognitive performance of the subjects described in this paper was fully within normal limits, and would likely be clinically characterized as inefficiencies rather than impairments.

Contrary to our initial hypothesis, psychiatric comorbidities did not have a significant influence on cognitive performance in this population of burn patients. However, a small association was observed between both a history of mTBI (3.6%) and use of narcotic pain medications (1.6%) and neurocognitive performance. The combined possible variables only accounted for 12.9% of the total variance in cognitive performance, and demographic characteristics accounted for the largest proportion of the variance (4.8%).

There are several limitations of the current study which merit discussion. Given the retrospective design of the study, psychiatric co-morbidity was determined via record review rather than using psychometric instruments. This methodology prevented analysis of the severity of psychiatric disturbance, a factor which has been shown to dramatically affect neuropsychological performance following mTBI [7]. This method also limited the identification of the specific psychiatric diagnosis or general classification (e.g., stress spectrum disorder versus mood disorder). Furthermore, given the overlap of psychiatric and post-concussive symptoms demonstrated in service members with burn injuries [10], it is possible that some post-concussive symptoms, such as irritability or sleep disturbance, could have been incorrectly attributed to a psychiatric condition or disorder.

Additionally, there is a limitation brought upon by the use of standard scores as the dependent measures

in this study. While the retrospective study design prohibited analysis of raw scores, the process of converting raw scores into “normalized” standard scores on the RBANS creates some additional problems. Specifically, measures of information processing speed and working memory, two separate cognitive constructs, are artificially merged during the normalization process to create the Attention Index [22]. While this strategy has some psychometric advantages in an instrument designed as a screening battery, it may have obscured important clinical information that differentiates between psychiatric (i.e., working memory difficulties) and neurological or pharmacological (i.e., slowed processing speed) effects. In addition, the RBANS is essentially a screening measure, and as such, may not be sufficiently sensitive to assess the broad range of neurocognitive difficulties following concussive injuries. Future studies need to continue to rigorously examine the relationship between psychiatric disorders, mTBI, and neurocognitive performance.

Consistent with prior studies of OIF/OEF service members with mTBI, a high percentage of brain-injured patients in the current study had co-morbid psychiatric conditions [11,12,24] and at a higher rate than in the TBI Negative group. It is unclear if this finding represents a causal, combinatorial, or spurious relationship. However, an important finding in the current study is that the interaction between TBI and psychiatric conditions did not significantly contribute to cognitive difficulties. The current conflicts in Iraq and Afghanistan allow for continued exploration of these issues. Better understanding of diagnostic comorbidities and potential interaction effects will hopefully lead to improved patient care and better clinical outcomes.

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