Characterization and Study of Acute Military Mild Traumatic Brain Injury in the War-Zone

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ASENT/ISCTM
Methodological Issues in Traumatic Brain Injury Research

Defense and Veterans Brain Injury Center

(originally the Defense and Veterans Head Injury Program, DVHIP)

The DVHIP was established in Feb 1992 and represented a unique collaboration among the DoD, VA, and civilian partners

Congressionally directed program with tri-fold mission

- Clinical Care
- Clinical Research
- Education

Added mission:

- Surveillance / Informing Force Management

Research Mission

To coordinate clinical research endeavors for TBI within the DoD and VA through prevention, diagnosis and treatment while emphasizing positive outcomes for this uniquely affected TBI population.

TBI is a common injury in OIF/OEF

Recently published TBI screening results:

- 16% of returning Army Soldiers screened positive[1]
- 15% of returning Army Soldiers screened positive[2]
- 19% of OIF/OEF Veterans screened positive[3]
- 23% of returning Army Soldiers screened positive[4]
- 18.5% of Veterans at VA medical centers screened positive[5]

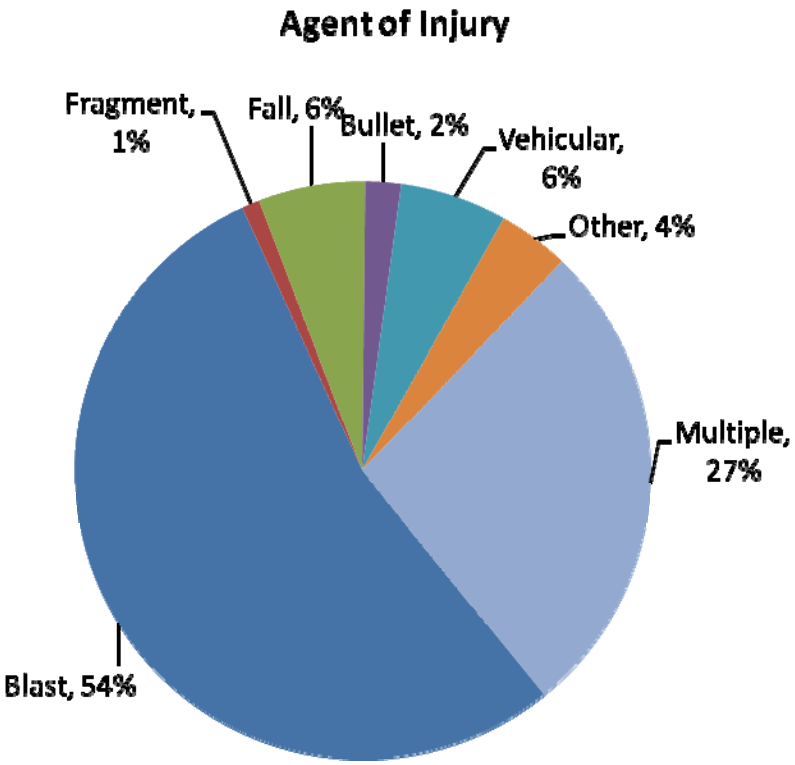
1. Schwab KA, Ivins B, Cramer G, Johnson W, Sluss-Tiller M, Kiley K, Lux W, Warden B. Screening for traumatic brain injury in troops returning from deployment in Afghanistan and Iraq: Initial investigation of the usefulness of a short screening tool for traumatic brain injury. *J Head Trauma Rehabil* 2007; 22(6): 377-389.
2. Hoge CW, McGuirk D, Thomas JL, Cox AL, Engel CC, Castro CA. Mild traumatic brain injury in US soldiers returning from Iraq. *N Engl J Med* 2008; 358(5): 453-463.
3. Schell TL, Marshall GN. Chapter 4, Survey of individuals previously deployed for OIF/OEF. In Tanielian T and Jaycox LH (eds.) *Invisible Wounds: Mental Health and Cognitive Care Needs of America's Returning Veterans*. Santa Monica, CA: The RAND Corporation; 2008.
4. Terrio H, Brenner LA, Ivins BJ, Cho JM. Helmick K, Schwab K, Scally K, Bretthauer R, Warden D. Traumatic brain injury screening: Preliminary findings in a US Army brigade combat team. *J Head Trauma Rehabil* 2009; 24(1): 14-23.
5. Unpublished data.

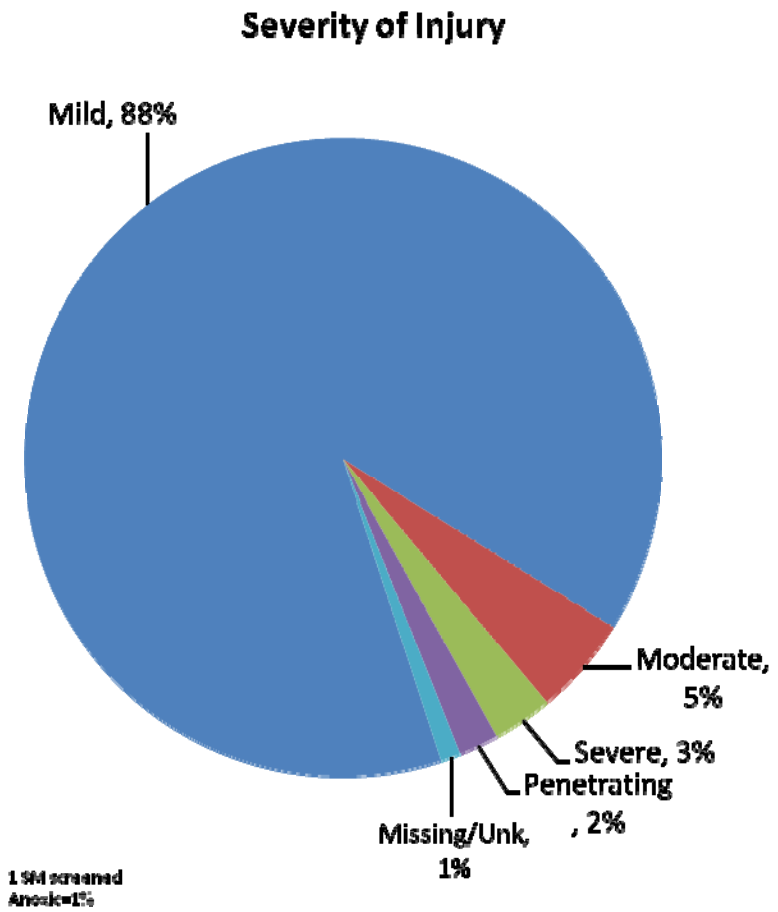
Why is TBI So Common in OIF/OEF?

- Improved Body Armor
  - o Increased survivability of injuries
- Increased awareness → Increased screening and detection
- Improved Combat Lifesaving techniques
  - o Tourniquet management
  - o Air Evac System

Characteristics of TBI in OIF/OEF

(n=8,687)





Source: Defense and Veterans Brain Injury Center. Data through October 31, 2008

Definitions of mTBI

ACRM definition of MTBI [1]

Traumatically induced physiological disruption of brain function that results in one or more of the following:

- Any alteration in mental state at time of injury
- Any loss of consciousness lasting 30 minutes or less
- Post traumatic amnesia lasting 24 hours or less

DoD definition of MTBI[2]

- Normal structural imaging
- Alteration of mental state lasting up to 24 hours
- Loss of consciousness lasting up to 30 minutes
- Post traumatic amnesia lasting up to 1 day

1.Kay T, Harrington DE, Adams R, Anderson T, Berrol S, Cicerone K, Dahlberg C, Gerber D, et al. Definition of mild traumatic brain injury. *J Head Trauma Rehabil* 1993; 8: 86-88.
2.Memorandum from the Assistant Secretary of Defense for Health Affairs, October 1, 2007.

Mild TBI/Concussion Case Definition

- Two conditions must be met to suspect/diagnose a TBI:
  - An injury must occur AND
  - The person must have experienced an alteration of consciousness (ranging from dazed or confused to amnesia to loss of consciousness)
  - In the absence of documentation, both of these are based on self reporting

Natural History of mTBI

General recovery time for MTBI[1]

- 7 to 10 days for very mild TBI
- Up to 3 months for more significant mTBI

Civilian studies have estimated that 5% to 20% of those with MTBI have problems that persist beyond 3 months, the so called “miserable minority”[2-4]

1.Alexander MP. Mild traumatic brain injury: Pathophysiology, natural history, and clinical management. *Neurology* 1995; 45: 1253-1260.
2.Iverson GL. Outcome from mild traumatic brain injury. *Curr Opin Psychiatry* 2005; 18: 301-317.
3.Alves W, Macciochi SN, Barth JT. Postconcussive symptoms after uncomplicated mild head injury. *J Head Trauma Rehabil* 1993; 8: 48-59.
4.Ruff RM, Camenzuli L, Muerller J. Miserable minority: emotional risk factors that influence the outcome of a mild traumatic brain injury. *Brain Inj* 1996; 10: 551-565.

Possible Consequences of mTBI on Service Members while In-Theater

- Slower reaction time
- Decreased concentration
- Slowed thinking

Unresolved mTBI-related impairments can increase the safety risks service members face when performing their missions in-theater

In-theater TBI Screening Process

Personnel involved in the following are screened as soon as possible after the event:

- Blast/Explosion
- Fall
- Vehicle crash
- Direct impact

In-theater mTBI Identification Tool

Military Acute Concussion Evaluation (MACE)

- Injury description with symptoms
- Includes the Standardized Assessment of Concussion (SAC)
    - Brief neurologic examination
    - Brief cognitive evaluation with alternate versions assessing
        - Orientation
        - Immediate memory
        - Concentration
        - Delayed Recall

In-theater mTBI Identification Tool

Military Acute Concussion Evaluation (MACE)

Patient Name: _____

SS#: _____-_____-_____Unit: _____

Date of Injury: ____/____/____ Time of Injury: _____

Examiner: _____

Date of Evaluation: ____/____/____ Time of Evaluation: ____

History: (I – VIII)

I. **Description of Incident**
Ask:
A) What happened?
B) Tell me what you remember.
C) Were you dazed, confused, "saw stars"? ❒ Yes ❒ No
D) Did you hit your head? ❒ Yes ❒ No

II. **Cause of Injury** (Circle all that apply):
1) Explosion/Blast 4) Fragment
2) Blunt Object 5) Fall
3) Motor Vehicle Crash 6) Gunshot wound
7) Other _____

III. **Was a helmet worn?** ❒ Yes ❒ No Type _____

IV. **Amnesia Before: Are there any events just BEFORE the injury that are not remembered? (Assess for continuous memory prior to injury.)**
❒ Yes ❒ No If yes, how long _____

V. **Amnesia After: Are there any events just AFTER the injuries that are not remembered? (Assess time until continuous memory after the injury.)**
❒ Yes ❒ No If yes, how long _____

VI. **Does the individual report loss of consciousness or "blacking out"?** ❒ Yes ❒ No If yes, how long _____

VII. **Did anyone observe a period of loss of consciousness or unresponsiveness?** ❒ Yes ❒ No If yes, how long _____

VIII. **Symptoms** (circle all that apply)

1) Headache
2) Dizziness
3) Memory Problems
4) Balance Problems
5) Nausea/Vomiting
6) Difficulty Concentrating
7) Irritability
8) Visual Disturbances
9) Ringing in the Ears
10) Other _____

Military Acute Concussion Evaluation (MACE)

Examination: (IX – XIII)

Evaluate each domain. Total possible score is 30.

IX. **Orientation:** (1 pt. each)

Month:	0	1
Date:	0	1
Day of Week:	0	1
Year:	0	1
Time:	0	1

Orientation Total Score _____/5

X. **Immediate Memory:**
Read all 5 words and ask the patient to recall them in any order. Repeat 2 more times for a total of 3 trials. (1 pt. for each correct, total over 3 trials)

List	Trial 1		Trial 2		Trial 3	
Elbow	0	1	0	1	0	1
Apple	0	1	0	1	0	1
Carpet	0	1	0	1	0	1
Saddle	0	1	0	1	0	1
Bubble	0	1	0	1	0	1
Trial Score						

Immediate Memory Total Score _____/15

XI. **Neurological Screening**
As the clinical condition permits, check
Eyes: pupillary response and tracking
Verbal: speech fluency and word finding
Motor: pronator drift, gait/coordination
Record any abnormalities. **No points are given for this.**

Military Acute Concussion Evaluation (MACE)

XII. **Concentration**
Reverse Digits: (go to next string length if correct on first trial. Stop if incorrect on both trials.) 1 pt. for each string length.

4-9-3	6-2-9	0	1
3-8-1-4	3-2-7-9	0	1
6-2-9-7-1	1-5-2-8-5	0	1
7-1-8-4-6-2	5-3-9-1-4-8	0	1

Months in reverse order: (1 pt. for entire sequence correct)
Dec-Nov-Oct-Sep-Aug-Jul-Jun-May-Apr-Mar-Feb-Jan

Concentration Total Score ____/5

XIII. **Delayed Recall (1 pt. each)**
Ask the patient to recall the 5 words from the earlier memory test. (Do NOT reread the word list.)

Elbow	0	1
Apple	0	1
Carpet	0	1
Saddle	0	1
Bubble	0	1

Delayed Recall Total Score ____/5
TOTAL SCORE _____/30

Notes: _____

_____

Diagnosis: (circle one or write in diagnoses)

No concussion
850.0 Concussion without Loss of Consciousness (LOC)
850.1 Concussion with Loss of Consciousness (LOC)

Other diagnoses _____

_____

In Theater Cognitive Assessment ANAM4™ TBI Battery

Test List	Domain/Function
Demographics	User Profile
TBI Questionnaire	TBI History
Sleepiness Scale	Fatigue
Mood Scale	Mood State
Simple Reaction Time	Basic neural processing (speed/efficiency) (Emphasis on motor activity)
Code Substitution – Learning	Associative Learning (speed/efficiency)
Procedural Reaction Time	Processing Speed (choice RT/rule)
Mathematical Processing	Working Memory
Matching to Sample	Visual Spatial Memory
Code Substitution – Delayed	Memory (delayed)
Simple Reaction Time (R)	Basic neural processing (speed/efficiency)

In-Theater Cognitive Assessment
ANAM4™ TBI Battery

Page 1

ANAM Performance Report

ID:	*****9999
Name:	SMITH, ROGER EDWARD
Rank:	PFC (E3)
Service:	ARMY
Status:	ACTIVE DUTY
Age: 20	Gender: M
Session: 03	

Test Date: August 14, 2007 3:11 PM
INJURY/EXPOSURE - DEPLOYMENT
Setting: ECHELON III

SUMMARY PERFORMANCE INDICATOR

Source: Baseline

AVERAGE OR ABOVE | BELOW AVERAGE | CLEARLY BELOW

DISCLAIMER
The information provided in this report does not represent medical advice, diagnosis, or a prescription for treatment. Providers should use these results in conjunction with a complete medical examination.*

HISTORY

Injury cause(s): Blast or Explosion

Resulting in: Dazed, confused, saw stars; Knocked out - 1 to 20 minutes; Did not remember the injury; Concussion symptoms

Symptoms Right after Injury: Headaches, Nausea / vomiting, Balance problems / dizziness

Symptoms Now at Rest: Headaches, Sleep problems, Irritability (short temper), Memory problems / lapses

Symptoms Now after Exertion: Balance problems / dizziness, Memory problems / lapses

PROVIDER OBSERVATIONS
MACE:
Interval between current and previous injury:

PERFORMANCE AT A GLANCE

Comparison Group: Military: Fort Campbell Males Age 18-25

Comparison to BASELINE	SCALE (DOMAIN)		AVERAGE OR ABOVE	BELOW AVERAGE	CLEARLY BELOW
-1.73	Simple Reaction Time	(REACTION TIME)			■
-3.09	Procedural Reaction Time	(PROCESSING SPEED)		■	
-1.95	Code Substitution - Learning	(LEARNING)		■	
-3.7	Code Substitution - Delayed	(DELAYED MEMORY)	■		
-2.64	Mathematical Processing	(WORKING MEMORY)	■		
-3.64	Matching to Sample	(SPATIAL MEMORY)		■	

SLEEP (1-7)
Score: 4 - A little tired and having mild difficulty concentrating.

MOOD (0-100)
28 HAPPINESS
31 VIGOR
72 FATIGUE
50 RESTLESSNESS
50 ANXIETY
42 DEPRESSION
61 ANGER

REFERENCE
Category lower limits for Below Average (9th percentile, 80.5 standard score) and Clearly Below Average (2nd percentile, 70 standard score) are based on Hannay, H. J., & Lezak, M. D. (2004). The neuropsychological examination: Interpretation. In M. D. Lezak, D. B. Howieson, & D. W. Loring (Eds.), *Neuropsychological Assessment* (pp. 133-156). New York: Oxford University Press.

*C-SHOP and the University of Oklahoma are not responsible for any decisions made based on information contained in the report. The provider has the sole responsibility for establishing diagnosis and suggesting appropriate treatment.

Page 2

ANAM Performance Report

ID:	*****9999
Name:	SMITH, ROGER EDWARD
Rank:	PFC (E3)
Service:	ARMY
Status:	ACTIVE DUTY
Age: 20	Gender: M
Session: 03	

Test Date: August 14, 2007 3:11 PM
INJURY/EXPOSURE - DEPLOYMENT
Setting: ECHELON III

SUMMARY PERFORMANCE INDICATOR

Source: Baseline

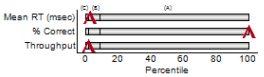
AVERAGE OR ABOVE | BELOW AVERAGE | CLEARLY BELOW

PERFORMANCE DETAIL

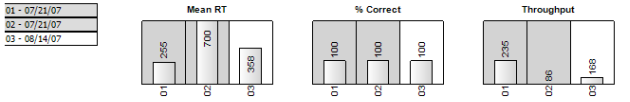
SIMPLE REACTION TIME (REACTION TIME) [8/14/2007, 3:15 PM]

Correct: 40 Incorrect: 0 Lapse: 0

	Score	%ile	StdSc	Comparison Group N	Mean	StDev
Mean RT (msec)	358	3	76	181	265	59
% Correct	100	100		181	100	0
Throughput	168	2	68	181	233	31



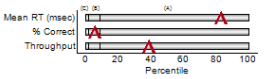
SIMPLE REACTION TIME (REACTION TIME) ARCHIVE



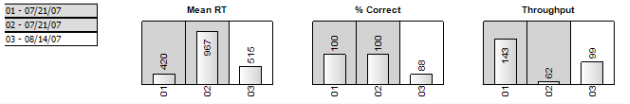
PROCEDURAL REACTION TIME (PROCESSING SPEED) [8/14/2007, 3:16 PM]

Correct: 28 Incorrect: 4 Lapse: 0

	Score	%ile	StdSc	Comparison Group N	Mean	StDev
Mean RT (msec)	515	83	110	182	583	102
% Correct	88	6	76	182	96	5
Throughput	99	39	98	182	101	15



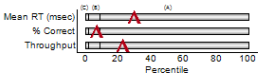
PROCEDURAL REACTION TIME (PROCESSING SPEED) ARCHIVE



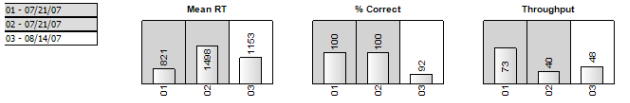
CODE SUBSTITUTION - LEARNING (LEARNING) [8/14/2007, 3:19 PM]

Correct: 66 Incorrect: 6 Lapse: 0

	Score	%ile	StdSc	Comparison Group N	Mean	StDev
Mean RT (msec)	1153	30	95	182	1077	230
% Correct	92	7	77	182	97	3
Throughput	48	23	89	182	56	11



CODE SUBSTITUTION - LEARNING (LEARNING) ARCHIVE



Basic Tenets of TBI Clinical Guideline

- Although uncommon, identify red flags that may prompt rapid triage and evacuation in a concussed patient.
- Early identification/detection of concussion is important so that treatment can begin
- Return to unrestricted duty when TBI related symptoms resolved
- Educate about concussion immediately after dx
- Rest and Education - cornerstones of management
  - Knowing how much recovery time is important
  - Exertional testing is a tool to determine RTD

Components of Guideline

- 3 algorithms for care
  - Combat medic/corpsman
  - Initial management of concussion
  - Comprehensive concussion algorithm
- Concussion information sheet (SM), FAQ format
- Duty restrictions
- TBI exertional testing procedures
- Accessing consultative services: tbi.consult

Definition Challenges Posed by mTBI

- Linking clinical phenomena (consciousness change) to physiological event (metabolic cascade)
- Loss of Consciousness
- Alteration of Consciousness

Clinical Challenges Posed by mTBI

- Understanding Blast as a Mechanism
  - Challenge of “Blast Plus”
- Psychological Co-Morbidities such as PTSD
- Early detection and treatment
  - Blast Detectors
- Return to Duty Decisions
  - Role of Computerized Cognitive Testing
  - Other Assessments (vestibular, etc.)
- Cumulative mTBI

Validity of MACE for TBI Screening

A recent study performed in Iraq provided preliminary evidence of the MACE's validity in a sample of blast injured service members with MTBI who were evaluated within 24 hours of injury[1]

- The MACE score correlated significantly with the duration of loss of consciousness (p=.013)
- The MACE score correlated significantly with the RBANS Immediate Memory factor (p=.014)

1.Grant G, Issler W, Baker M, Erlanger D, Kaushik T. Preliminary validation of the MACE. Unpublished data.

“Head to Head” Study Brief Computerized Cognitive Assessment Batteries

- Location: Falujah, Iraq
- Purpose: Compare in theater results to CONUS results.
- Compare TBI characteristics with cognitive results.
- Collaboration with USUHS
- Abr battery: Symptoms, combat experience, injuries
- Service members receiving clinical care in-theater for
    - TBI
    - Randomly assigned to receive 1 of 5 test batteries
    - All receive subset of neuropsychological evaluations
    - Stratified to match on injury severity, other injuries, and time since injury

Methodological Issues for In-Theater Studies

- Performing research studies in-theater, especially clinical trials, is very challenging

- Many methodological difficulties routinely encountered in other settings are exacerbated in-theater

Methodological Issues for In-Theater Studies

Difficulty accessing populations

- Mission supersedes all other activities
- Most service members based far from study sites
- Unwillingness by many to seek treatment for mTBI
- Concerns about pressure to participate

Obtaining uninjured controls will be greatest difficulty

Methodological Issues for In-Theater Studies

Numerous potential confounders

- Sleep deprivation
- Hyper-arousal
- Psychiatric comorbidites
- Other injuries

Methodological Issues for In-Theater Studies

Heightened safety concerns for clinical trials

Many medication side effects acceptable in civilian studies could be dangerous in a combat-environment

- Drowsiness
- Slowed reaction time