Studies of Chronic Problems after Mild TBI in Military Populations: Challenges in the Characterization of Chronic Problems and Design of Treatment Trials

Karen A. Schwab, PhD
Defense and Veterans Brain Injury Center

Brian Ivins, MS
Defense and Veterans Brain Injury Center

March 4, 2009
ASENT/ISCTM
Methodological Issues in Traumatic Brain Injury Research

The views expressed in this presentation are those of the author(s) and do not reflect the official policy of the Department of Defense or U.S. Government.

Talk Overview

- Challenges in identification of returning service members with mild TBI
- Symptoms and Problems: mild TBI or?
- Challenges in Conducting Treatment Trials

Implications of MTBI/Concussion

- Unit Readiness
  - 100 msec. – relatively large reaction time change
  - soldiers may be unable to will away symptoms
  - behavioral issues may ensue
- Individual Issues
  - feel “broken”
  - possible shell shock as repeat blast MTBI exposure
  - irritability/ issues with family and others

Challenges in Identifying Chronic Mild TBI

- Inadequacy of traditional methods (ICD codes, medical charts)
- Screening of returning service members

Diagnoses Considered to be TBI

ICD-9 CM Codes	Code Description
800.00-800.99	Fracture of vault of skull
801.00-801.99	Fracture of base of skull
803.00-803.99	Other and unqualified skull factures
804.00-804.99	Multiple fractures involving skull or face with other bones
850.0-850.9	Concussion
851.00-851.99	Cerebral laceration and contusion
852.00-852.59	Subarachnoid, subdural, and extradural hemorrhage following injury
853.00-853.19	Other and unspecified intracranial hemorrhage following injury
854.00-854.19	Intracranial injury of other and unspecified nature
854.00-854.19	Intracranial injury of other and unspecified nature
959.01	Head injury, unspecified

Estimates of Untreated TBI Cases

Sosin, Sniezek, and Thurman conservatively estimated from the 1991 National Health Interview Survey that 25% of TBI cases were medically untreated.*

* Brain injury was defined as self-reported head injury with loss of consciousness that also resulted in a period of restricted activity.

Missed TBI Diagnoses

51% of 47 patients seen in a British trauma center with a TBI did not have a TBI diagnosis recorded

Most TBI patients lacking a coded TBI diagnosis had other injuries coded

*TBI defined as any injury to the head *and* some gap in memory for events.

Moss NEG, Wade DT. Admission after head injury: How many occur and how many are recorded?. *Injury*. 1996; 27(3): 159-161.

Post Deployment TBI Questions + Symptoms

Did you have any injury(ies) during your deployment from any of the following? (check all that apply):

1. Fragment
2. Bullet
3. Vehicular (any type of vehicle, including airplane)
4. Fall
5. Blast (Improvised Explosive Device, RPG, Land mine, Grenade, etc.)
6. Other specify:

Did any injury received while you were deployed result in any of the following? (check all that apply):

1. Being dazed, confused or "seeing stars"
2. Not remembering the injury
3. Losing consciousness (knocked out) for less than a minute
4. Losing consciousness for 1-20 minutes
5. Losing consciousness for longer than 20 minutes
6. Having any symptoms of concussion afterward (such as headache, dizziness, irritability, etc.)
7. Head Injury
8. None of the above (any of 1-5 suggest a MTBI diagnosis by ACRM criteria)

Post-Deployment TBI Screening

- DVBIC has worked with multiple sites screening returning war fighters
- Approximately 10-20% war fighters had a TBI while in theater (Army Times-Sept 5, 2005)
- Virtually all were mild TBI

Morbidity of TBI

Cognitive, Somatic, Neuropsychiatric sequelae

Postconcussion Symptoms (PCS)

- Headache
- Dizziness
- Irritability
- Decreased Concentration
- Memory Problems
- Fatigue
- Visual Disturbances
- Sensitivity to Noise
- Judgment Problems
- Anxiety
- Depression

Post Concussive Sx in Mild TBI

- Natural history is recovery within weeks to months (Levin 1987), although a small percentage will continue to have persistent symptoms (Alexander, Neurology 1995)
- High school athletes with 3 or more prior concussions were up to 9 times more likely to develop symptoms than athletes without prior injury (Collins, et al, Neurosurgery 2004)
- Patients with MTBI may be more sensitive to symptoms/dysfunction than their families; patients with moderate-severe TBI are less sensitive to dysfunction than their families (Drake, et al, unpublished data)

Average Number of Post TBI Symptoms by Severity of Injury: Ft. Bragg

(For those reporting on 20 or more of the 22 symptoms)

Severity of Prior TBI	Average Number of Symptoms
No TBI (n=687)	2.00
Altered Mental State Only (n=281)	3.41
1-20 mins LOC (n=296)	4.24
21-59 mins LOC (n=40)	5.58
1 hr or more LOC (n=30)	5.90

Neurocognitive Changes

Attention/Concentration

Speed of Mental Processing

Learning/Information Retrieval

Executive Functions (e. g., Planning, Problem Solving, Self Monitoring) May see judgment problems, apathy, inappropriate behaviors

Psychological/Psychiatric and Psychosocial Changes after TBI

Personality:

- Increased/Decreased Activation
- Episodic Dyscontrol;Irritability

Psychiatric:

- Mood Disturbance
- Psychosis

Psychosocial:

- Work Status
- Relationships with others

Depression and TBI

- Approximately 33% of hospitalized TBI patients develop Major Depression in 1st year (Jorge et al 2004)
- 25-60% of TBI patients develop a depressive episode within 8 years of injury (Kreutzer, 2001; Hibbard, et al, 1998; Jorge and Robinson, 2002).
- Depression is associated with comorbid anxiety, aggressive behavior, poorer social and functional outcome (Jorge and Robinson, 2002; Jorge et al 2004) and left frontal brain injury; Jorge et al 2004).

Post Deployment Data: Fort Carson SRC, 2004

Percent of Soldiers with Clinician Confirmed TBI Reporting 1 or More Symptoms:

Right after Injury: 92%

At time of return from deployment: 39%

Total N Screened: 3973

Total N with Clinician Confirmed TBI: 907

Terrio, et al, Traumatic Brain Injury Screening: Preliminary Findings in a US Army Brigade Combat Team, J Head Trauma Rehabil, Vol 24, pp. 14-23 (2009)

Morbidity of TBI

Symptoms and Problems Post Mild TBI:*

Mild TBI or Associated Injuries and Co-Morbid Conditions?

- PTSD
- Depression
- Other Injuries
- Pain
- Multiple Deployments = Multiple Exposures

Treatment Trials for Mild TBI

Challenges in Conducting Treatment Trials:

Limited Evidence to date

Recruitment

Randomization

Complexities: multiple deployments, co-morbidities, issue of pharmaceutical treatments on board.

Introduction

- Individuals with Traumatic Brain Injury (TBI) generally improve over time.
- All treatments, therefore, seem to work.
- Need for well-controlled studies with standardized evaluation instrument, outcome measures, well-specified treatments, and control groups.
- Randomization into treatments (RCTs) lessens the impact of certain biases that can plague other studies.
- RCTs can provide reliable evidence on the efficacy of drug treatments, non-pharmaceutical rehabilitation treatments, and prevention approaches.

TBI Treatment

Pharmacotherapy:

Symptomatic Treatment: Headache, Sleep, Irritability

Antidepressants (e.g., SSRI's); PTSD

Stimulants

Anticonvulsants/Mood Stabilizers

Note: Limited Class I evidence to date; DVBIC RCT's in progress for SSRI's; Difficulties of completing in chronic symptomatic milds (drugs on board, difficulties recruiting)

TBI Treatment

Psycho-educational:

- TBI Symtomatology *
- Expected Course of Recovery *
  - With acute intervention, results show reduced morbidity

Rehabilitation:

- More intensive TBI rehabilitation when needed for more severe injuries (either in specialized centers or with TBI specialists in DVA or military centers; Salazar, et al., 2000)

Note: Evidence-Based (*Ponsford, et al., 2002; Mittenberg, et al., 1996; Bell, et al., in pressSalazar, et al., 2000;)

The Past Decade

1992 - "Large Randomized Trials can't be done in rehabilitation"

2000 – JAMA publication of WRAMC Randomized Controlled Trial of Cognitive Therapy for moderate-severe TBI

Features of RCTs that Discourage Use

- 1. Resource intensive
- 2. Design phase lengthy (DVBIC 1 to 2.5 years!)
- 3. IRB approval can take over a year – esp. in multi-center trials
- 4. No obvious sponsor for non-pharmaceutical treatments
- 5. Blinding difficulties – challenges for patient recruitment.
- 6. Perception that RCTs futile – Pharmaceutical Studies

Randomization

- Problems:
  - Clinician Guessing Game
  - Lobbying by Patients
- Solutions:
  - Independent Randomization
  - Concealment of Future Patient Assignments
  - Blocking (Randomized Block Sizes)

Recruitment

- “50% Rule”
- Referral Patterns - Difficult to Alter
- Military Turn-over/VA Reorganization
- Patient Transportation
- Patient Consent
- Clinical Research is Partnership between Patient, Family, Clinician, and Clinical Researcher

Conclusions

- Need well-controlled studies, including RCTs, in TBI Rehabilitation
- Should not wait for “total” information before begin
- Need trials on pharmaceutical management, other rehabilitation strategies, and prevention approaches
- One trial will probably not provide definitive evidence: replication, and studies of different treatments, different populations, and with different research methodologies are required.

Summary

- TBI in the current combat environment: not uncommon, often in association with severe multi-trauma, PTSD, or underdiagnosed concussion
- Possible consequences:
  - Effects on unit readiness when service members prematurely returned to duty
  - Lack of care can lead to increased morbidity
- Effective treatment requires identification of cases