

Explosive Blast Traumatic Brain Injury

Geoffrey Ling, M.D., Ph.D.

Colonel, Medical Corps, US Army

Program Manager, DARPA

Professor and Vice-Chair, Neurology, USUHS

Director, Neuro Critical Care, WRAMC

Associate Professor (adjunct), Anesthesiology & Critical Care Medicine,
Johns Hopkins

TBI in Modern Warfare

- Traumatic brain injury remains a leading cause of death and disability
- Historically, head injury accounts for 15-20% of battle related casualties
 - 50% of patients who died of wounds (DOW)
- Today, estimates of head injury is about 15%

Carey, Milt Med 152: 6 (1987)

Progmet et al, Milt Med 163: 482 (1998)

Navy-Marine Combat Casualty Registry (2005)

JTTR, Nov 2007

MORE THAN WE THINK?

- 25-40% OIF soldiers may have suffered closed head injury
- Many (how many?) may have suffered more than one such injury
- Many (how many?) may have persistent subtle neurological symptoms (> 6 months)
 - Estimates of 20-40% of exposed patients

Mechanisms of Traumatic Brain Injury

Penetrating Injury

Cause: Physical disruption of cells and fiber tracks, hemorrhaging, cell apoptosis

Concussive Injury

Cause: Mechanical loading leading to cell failure

Hypoxia

Cause: Lack of O₂

Explosive Blast Injury

Cause: Mechanism of injury **unknown**

STATISTICS

- Unprecedented survival:
7.5 WIA:1.0 KIA
- IED blast related injuries
significant source of
casualty admissions
- Head Trauma - when
compared to previous
conflicts
 - Increased #
Hemicraniectomies
 - Increased #
Neurovascular Injury
 - Increased # Complex
Cranial-facial Injuries

Newsweek, 2005

Armondo, WRAMC, 2006

Explosive Blast Injury - Categories

Four categories of blast injury:

- **Primary** – Caused by the direct blast energy
 - Crush injuries, lacerations, hemorrhage common
- **Secondary** – Caused by projectiles and other hazards created by the blast
 - Rubble, building fragments, shrapnel, etc.
- **Tertiary** – Inertial injuries caused by personnel being propelled by the blast (being thrown)
- **Quaternary** – Inhalation, burns, and anything else not described by first three

Explosive Blast TBI

Wide spectrum of neurological effects have been described

■ Mild TBI

- Subtle cognitive deficits, neurobehavior changes, mood and affect issues
- Both can occur together

■ Moderate TBI

- Loss of consciousness, overt structural damage

■ Severe TBI

- Severe neurological deficits, subarachnoid hemorrhage, vascular changes (acute and chronic)

Mild Traumatic Brain Injury

Traumatic brain injury symptoms

- Cognitive deficits
- Restlessness
- Behavioral affect
- Anxiety/increased stress levels
- Vertigo/loss of balance

“A growing number of U.S. troops whose body armor helped them survive bomb and rocket attacks are suffering brain damage as a result of the blasts ... The wound may come to characterize this war, much the way illnesses from Agent Orange typified the Vietnam War ” – *USA Today*, 3 Feb, 2005

“Thirty percent of U.S. troops surveyed have developed ... mental health problems three to four months after coming home from the Iraq war... The survey of 1,000 troops found problems... anxiety... anger and an inability to concentrate, said Lt. Gen. Kevin Kiley” – *Washington Post*, 29 July, 2005

(Some are trying to make the case that these symptoms are mild TBI)

“New TBI” versus PTSD

Mild Blast TBI

- Difficulty sleeping
- Emotional lability
- Difficulty concentrating
- Decreased appetite
- Other:
 - May have post-concussive syndrome (headaches, etc)

PTSD

- Sleep disturbance
- Outbursts of anger
- Difficulty concentrating
- Hypervigilance
- Exaggerated startle
- Other:
 - Re-experience
 - Avoidance

DSM-IV

Severe Blast TBI

- Severe early cerebral edema
- Diffuse hyperemia
- Delayed vasospasm
 - 10 – 14 days after initial injury
- SAH

In adversity, there is opportunity

Advances in Neurotrauma medical care

- Guideline directed pre-hospital TBI management
- Early decompressive hemicraniectomy
- Hypertonic brain resuscitation fluids
- Guideline directed in-hospital TBI management
- Appropriate use of vasopressors
- Transcranial Doppler at Echelon 3
- Neurovascular diagnostics
- Endovascular intervention

What Happens to TBI Survivors?

- 14.3% (n=8574) of soldiers injured in Vietnam had moderate to severe TBI
- Of 160 of the surviving TBI patients following prospectively from Vietnam:
 - 74% could live independently
 - 59 % are active in their community
- Early evidence from OIF/OEF is a higher percentage of survivors from initial TBI with better functional outcome

What is the mechanism of
injury?

Returning to first principles

Present State of the Art

■ Need to Know More

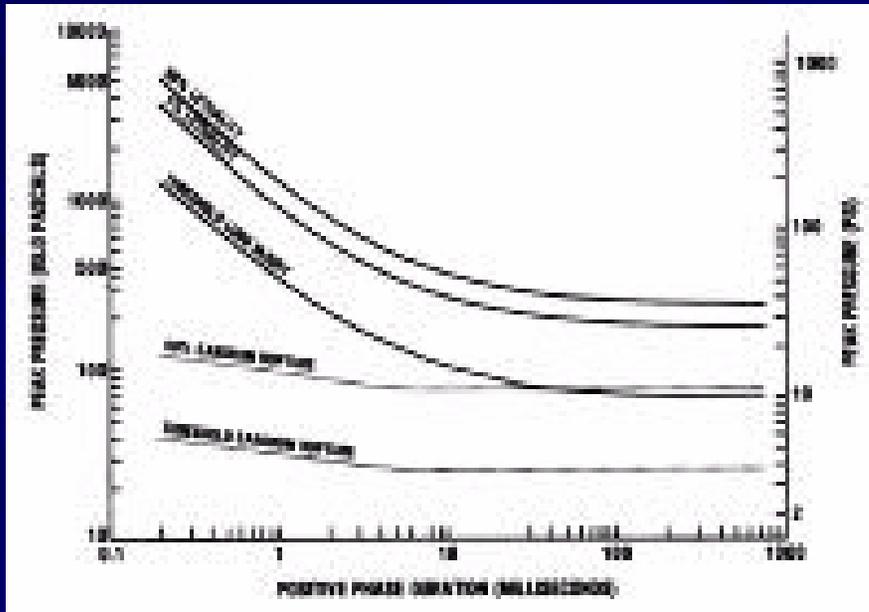
- Incomplete info about helmet performance
- Incomplete diagnosis
- No specific TBI treatments of any kind

■ Currently, the assumption is injury results from blast “overpressure”

- Is this the complete story?

State of the Art

Bowen-Richmond Curves



•Current metrics of blast injury are

- Binary: alive or dead
- Evaluate pressure damage to the lungs
- Do not address TBI

Some unstudied characteristics of explosions:

- Rapid temperature change
- Environmental chemical composition changes
- Electromagnetic pulse
- Kinetic energy transfer

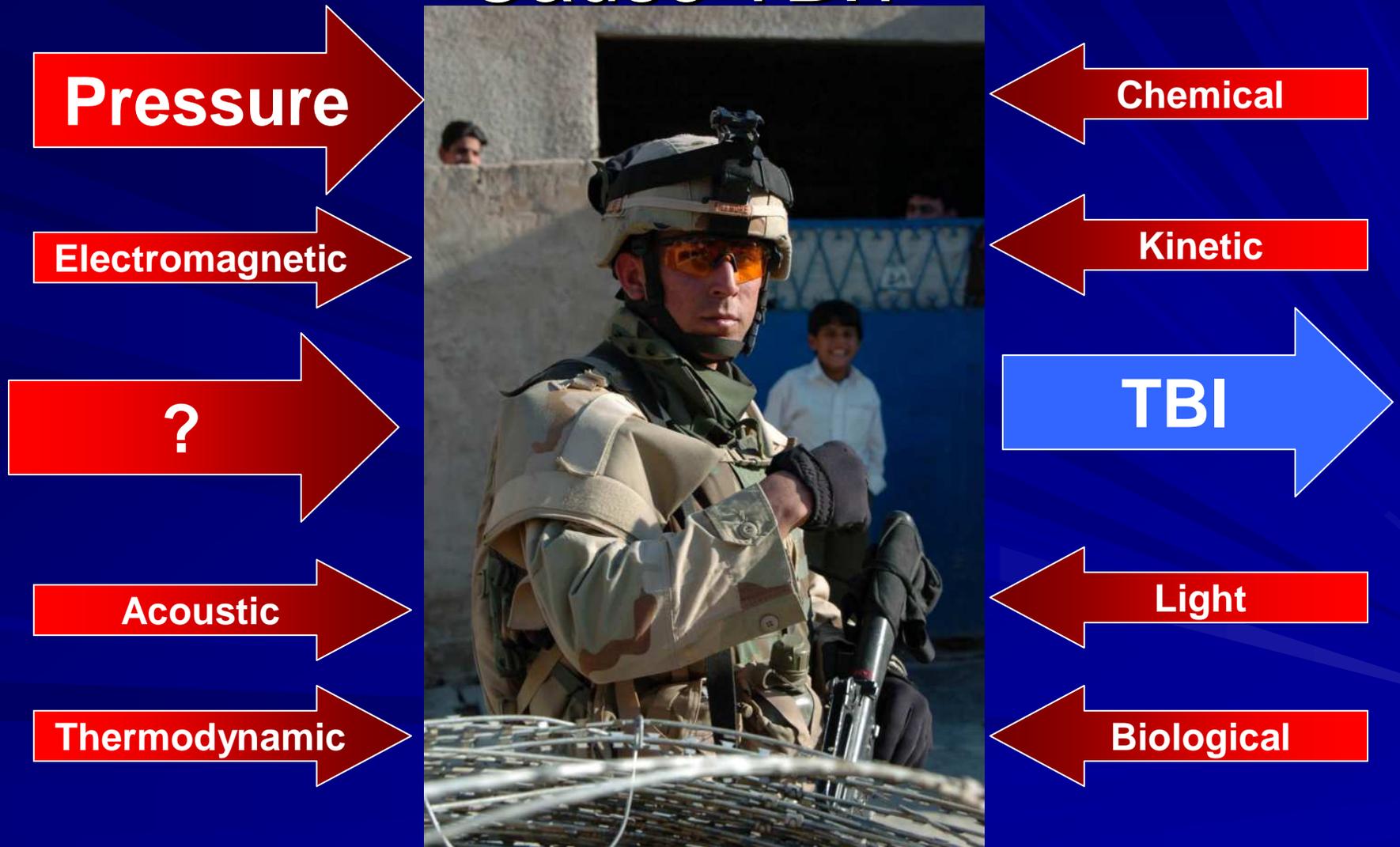
Paradox

- Many blast related TBI cases
- Few blast lung cases in isolation
- Few blast bowel cases

Rigorous Research Needed

Evidence to provide basis for
assumptions

What Elements of Explosions Can Cause TBI?



PREventing Violent Explosion Neurological Trauma (PREVENT)

A DARPA Program



Vision – PREVENT

Vision: Protecting soldiers from Traumatic Brain Injury through understanding the effects of explosive blast components

Phase I (12 Mo.)

Milestone:

- Identify physical mechanism (overpressure, EMP, etc.) and biological mechanism (apoptosis, etc.) of neurologic injury caused by explosion

Metrics:

- Histology
- damage to cell
- axonal death and damage
- Epidemiology
- # of animals affected in standard environment and at different ranges
- Cognitive impairment
- Ability to perform cognitive tests
- Appetite
- Functional impairment
- Gait/movement
- Sleep patterns

TWO



Phase II (18 Mo.)

Milestones:

- Refine Model
- Develop strategies, devices, and treatments to prevent injury from blast

Metric:

- Prevention of injury as defined by achieving an injury severity score reduction of > 50%

PREVENT: 2 Arms

Scientific Exploration
(WRAIR Team)

Explore injury mechanisms in

- Pig
- Tissue
- Epidemiological data

Clinical Arm
(Quantico Breacher
Study)

Unique cohort of Marines
•Repeated exposure to
blasts at varying
distance and magnitude



Descriptive Model:
(Phase 1 Deliverable)

Determines causes of injury

- Improve operations (tactics and training)
- Improve mitigation (armor, helmet)
- Improve medicine (clinical and pharmacological treatment)

Pre-Clinical



■ Pigs (Cumulative model)

- 8 animals per group
- Multiple distances, environments and explosive strengths

– Component model

- 12 animals per group
- Exposure to elements of blast sequentially in order to reproduce injury observed in cumulative model

■ Epidemiological database

– Markers of injury

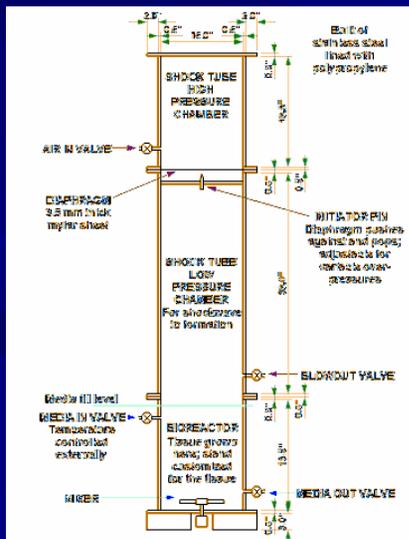
- Physiological
- Neurological
- Neurobehavioral

– Forensic information

- Used to supplement clinical markers

■ Tissue study

- Blast bioreactor
- Allows for studies of molecular and cellular response in immediate acute phase



Comprehensive testing by experienced specialists

- Unique bioreactor designed by Dr. K. Parker (Harvard)
- Porcine experiments developed by seeding performer S. Parks (ORA, inc.) who originally demonstrated absence of blast injury from overpressure alone

FOUO

Exposure

Exposure testing will be carried out and monitored with the assistance of Special Forces

- Tests conducted at appropriate test sties
- Operationally relevant scenarios will guide placement of subjects and level of charge
- Sensors used have been proven to be rugged and robust in previous blast testing

■ Thermal

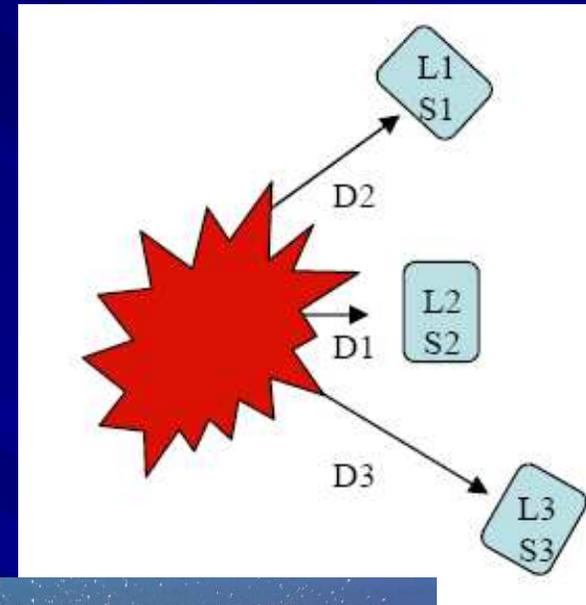
- Plasma and ejecta effects: heat depositions in tissue may lead to protein denaturing

■ Overpressure

- Peak overpressure
- Impulse
- Complex wave

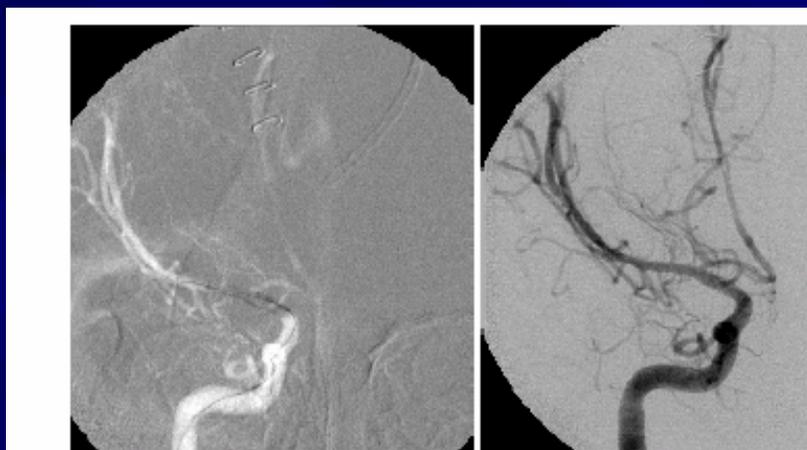
■ Electromagnetic band

- EMP Pulses exceeding levels where continuous fields have been shown to cause neurologic damage
 - Radio frequencies
 - Optical frequencies



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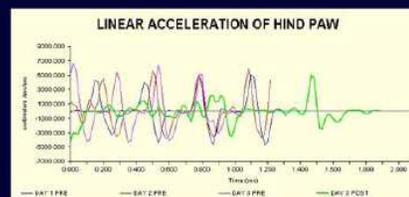
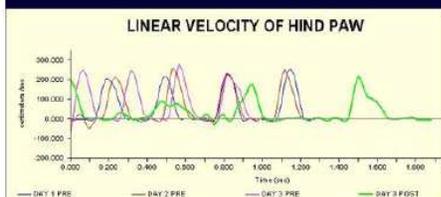
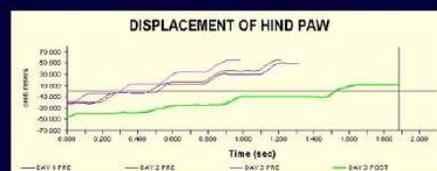
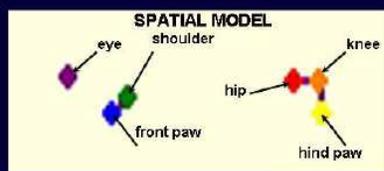
Outcomes



- EEG
- Neurocognition
 - Maze test
- Vasospasm
- Behavioral changes
 - Feeding
 - Sleep
- Neurologic
 - Gait tested as a measure of motor function disruption
- Histopathology

Comprehensive testing by experienced specialists

- Cognitive/Neurologic testing (WRAIR) – Developed by investigator
- Histology and pathology of injury (WRAMC) – Conducted by neurosurgeons with experience treating blast injured patients
- Collaborators include leading civilian TBI investigators



Unique Cohort Study

- Each Trainee exposed to:
- A) Pure Explosive Blast
 - B) > 50 exposures over 2 week course
 - C) Exposed to 20 grams – 5 lbs TNT eq.
 - D) Free field and enclosed environment

Trainees report:
Difficulty concentrating
Mood changes
Insomnia



Proposed Study:

40 Subjects;
28 exposed to explosion,
12 not exposed

Pre: Neurological testing,
Cognitive testing, Neuroimaging,
Mood/sleep diary

1 Week (Mid-course):
Neurological testing, Cognitive testing

2 Week (Post-course):
Neurological testing, Cognitive testing, Neuroimaging, review mood/sleep diary

3 Mo. (Post-course): Continue mood/sleep diary, neuroimaging and neurological and cognitive tests on available marines

FOUO