Report on TBI External Advisory Subcommittee to DHB

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TBI Component of Defense Center of Excellence for PH and TBI

Outline

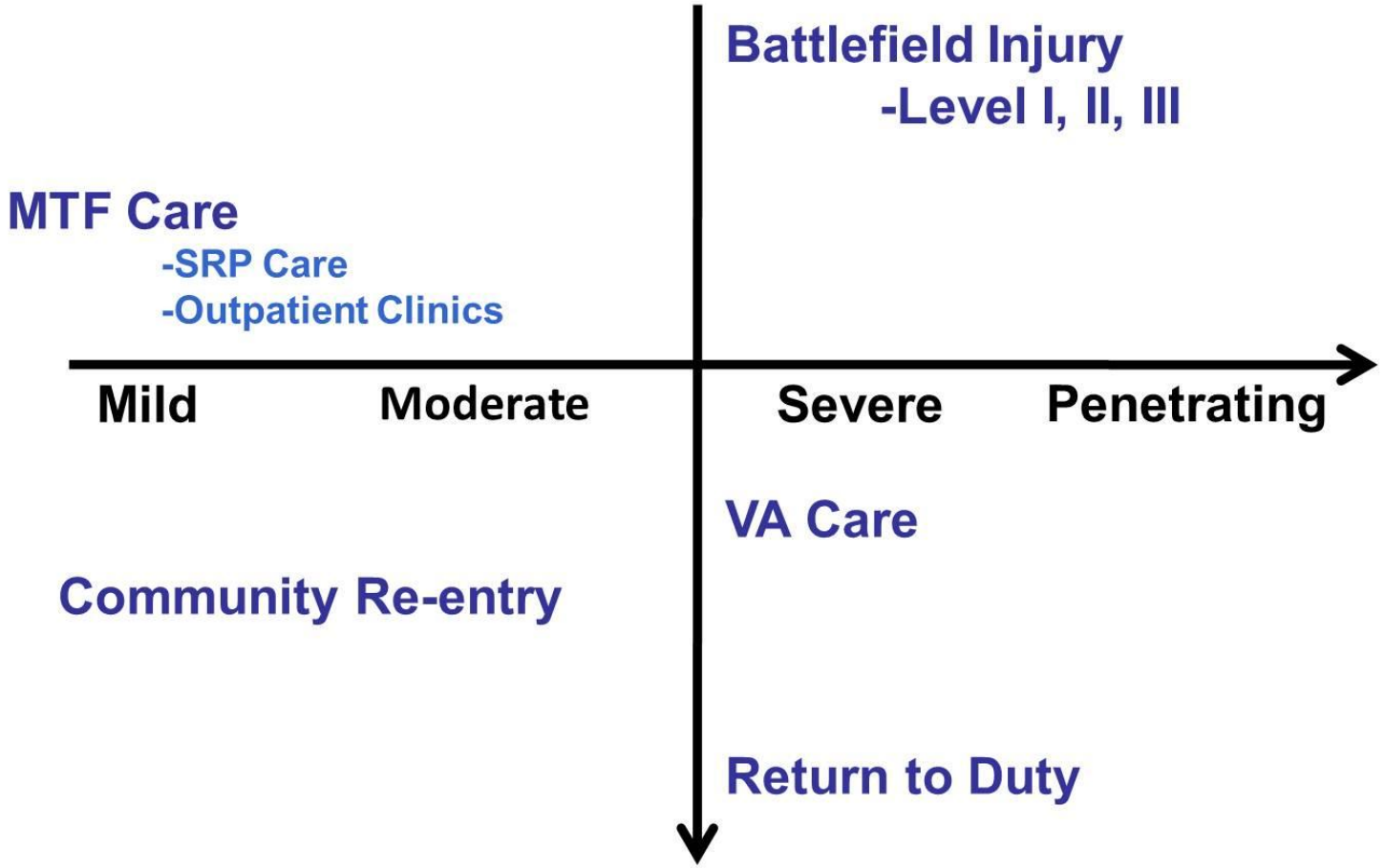
- Overview of DoD TBI Organization
- Summary of Challenges
  - Scientific Debates
  - Policy Challenges
- DHB TBI External Advisory Subcommittee
- Preliminary Plans for TBI Subcommittee

Scope of the Problem

- 31,760 wounded in OIF/OEF (ww.dod.mil, April 22, 2008)
- 66% of wounded in OIF are from Blast Injury (JTTS)
- Of soldiers exposed to a blast –
  - 41% have evidence of TBI (JTTS)
- TBI =32% of battle injuries seen at WRAMC from recent conflict (DVBIC data as of 02/29/08)
- 21% of Air Evac Patient from OIF had at least 1 head/neck trauma code

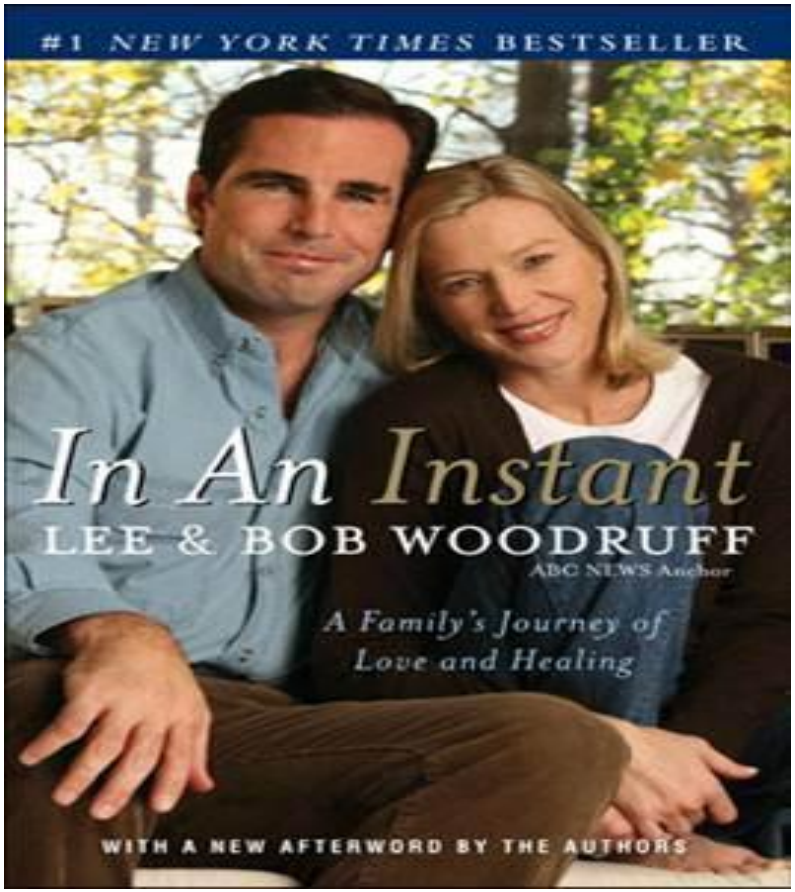
Mild: 85% Moderate: 7% Severe: 4% Penetrating: 3% Unknown: 1%

TBI - Deep & Wide

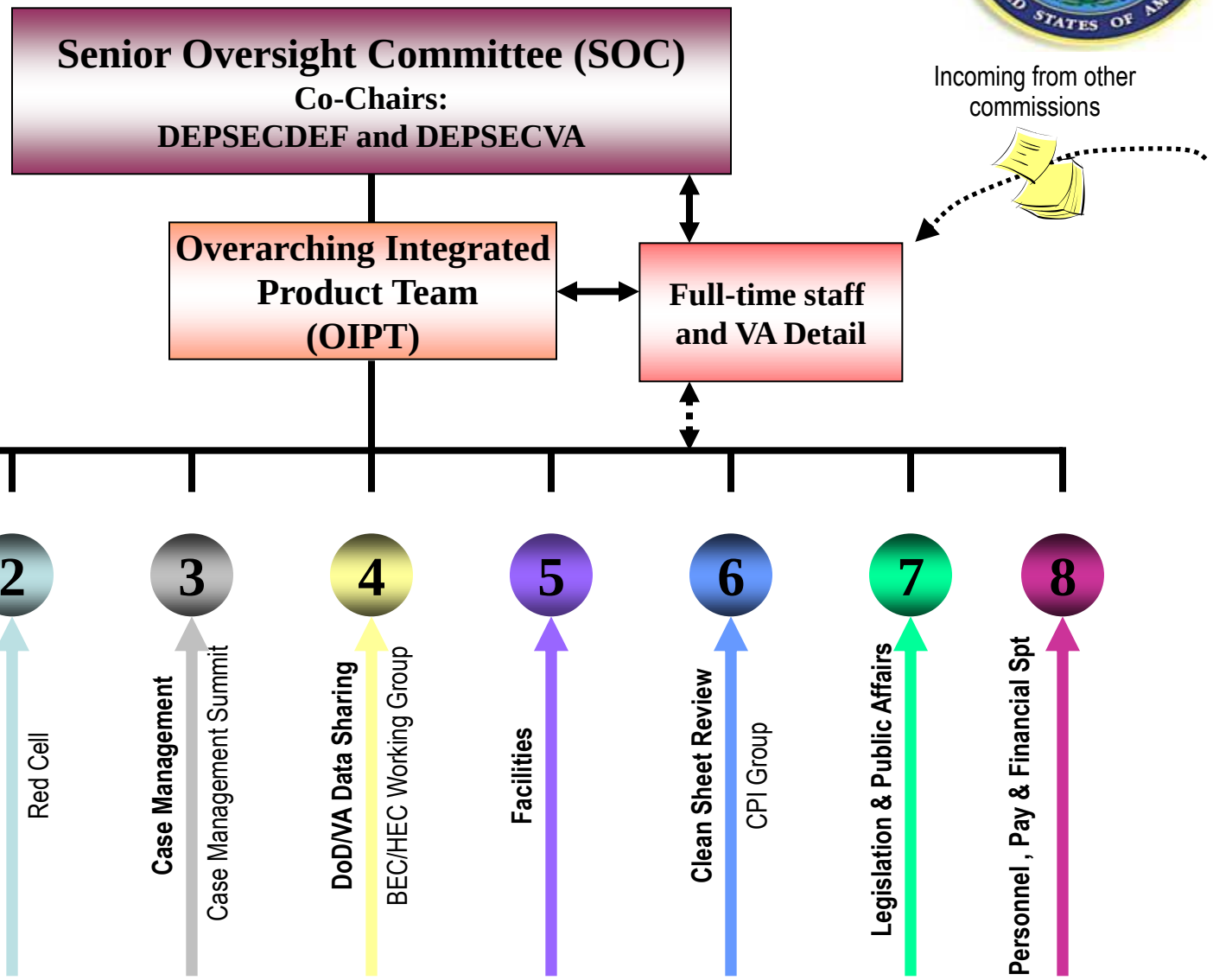


High-Level Attention

Increased Public Awareness



The Structure



As of June 29, 2007

TBI/PH Red Cell

- Authorized by FY 2006 National Defense Authorization Act

- Project list and program plan guided by
  - Commission / Reports
    - Independent Review Group (“Walter Reed”)
    - Presidents Commission (“Dole-Shalela”)
    - GWOT
    - Task Forces
  - Summits
    - Mental Health
    - DoD/DVA TBI x 2

DCoE Component Organizations

DVBIC
- Defense and Veterans Brain Injury Center

CDP
- Center For Deployment Psychology

DHCC
- Deployment Health Clinical Center

CSTS
- Center For The Study Of Traumatic Stress

NICoE
- National Intrepid Center of Excellence for PH and TBI

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 the Brain Injury Association (BIA).

Congressionally directed program

- Clinical Care
- Clinical Research
- Education

Per OSD / Health Affairs

Surveillance / Force Management

Predeployment Cognitive Testing

For the Active Duty Soldier,
Military Beneficiary and Veteran

DVBIC Initiative and Mission Statement

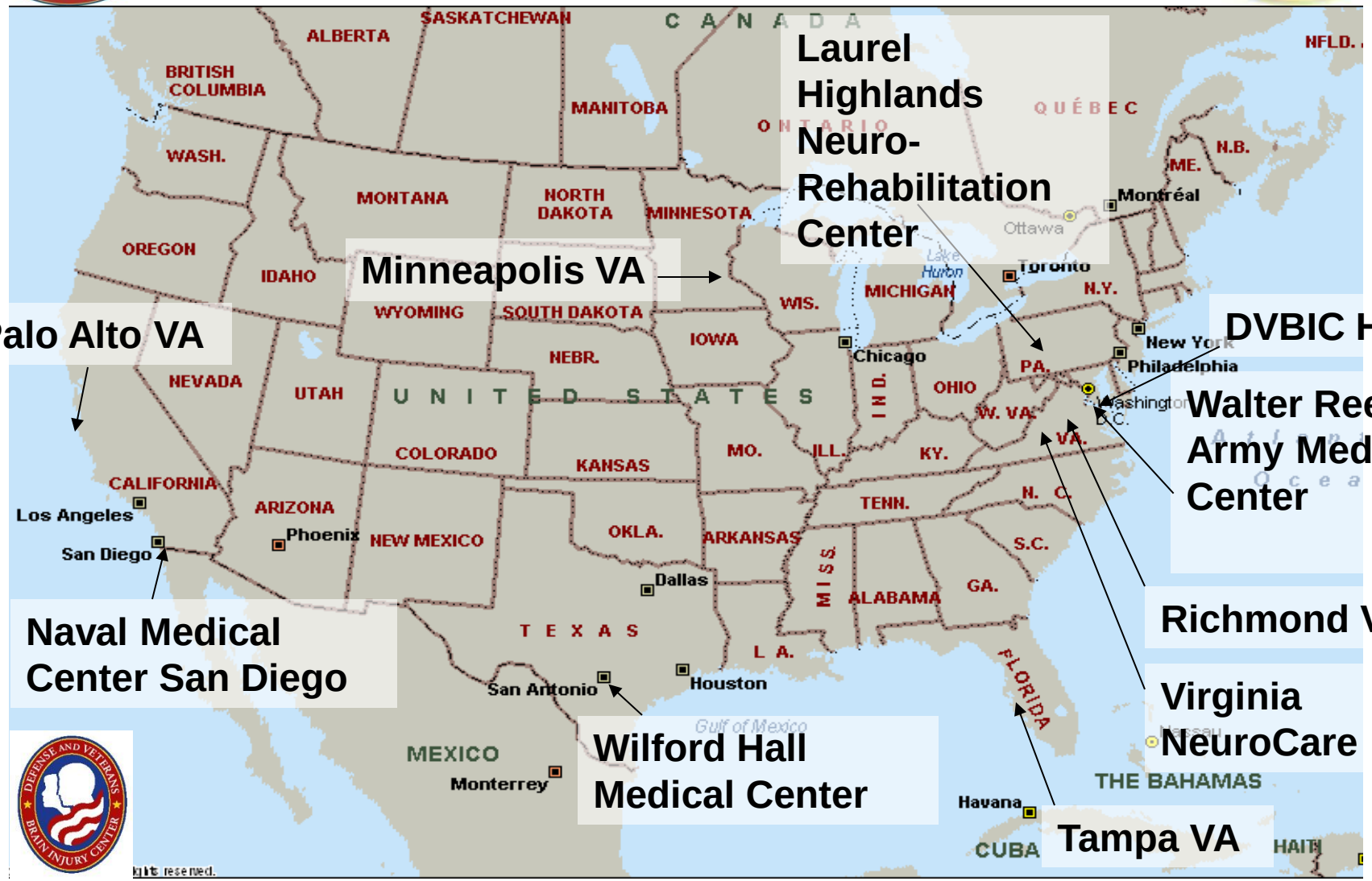
"This funding will be for [DoD to take the lead] in tracking and evaluating head injury survivors, ensuring that the survivor is getting appropriate treatment, studying the outcome of the treatment, and for counseling family members of the survivor."

DoD Appropriations Bill, 1991

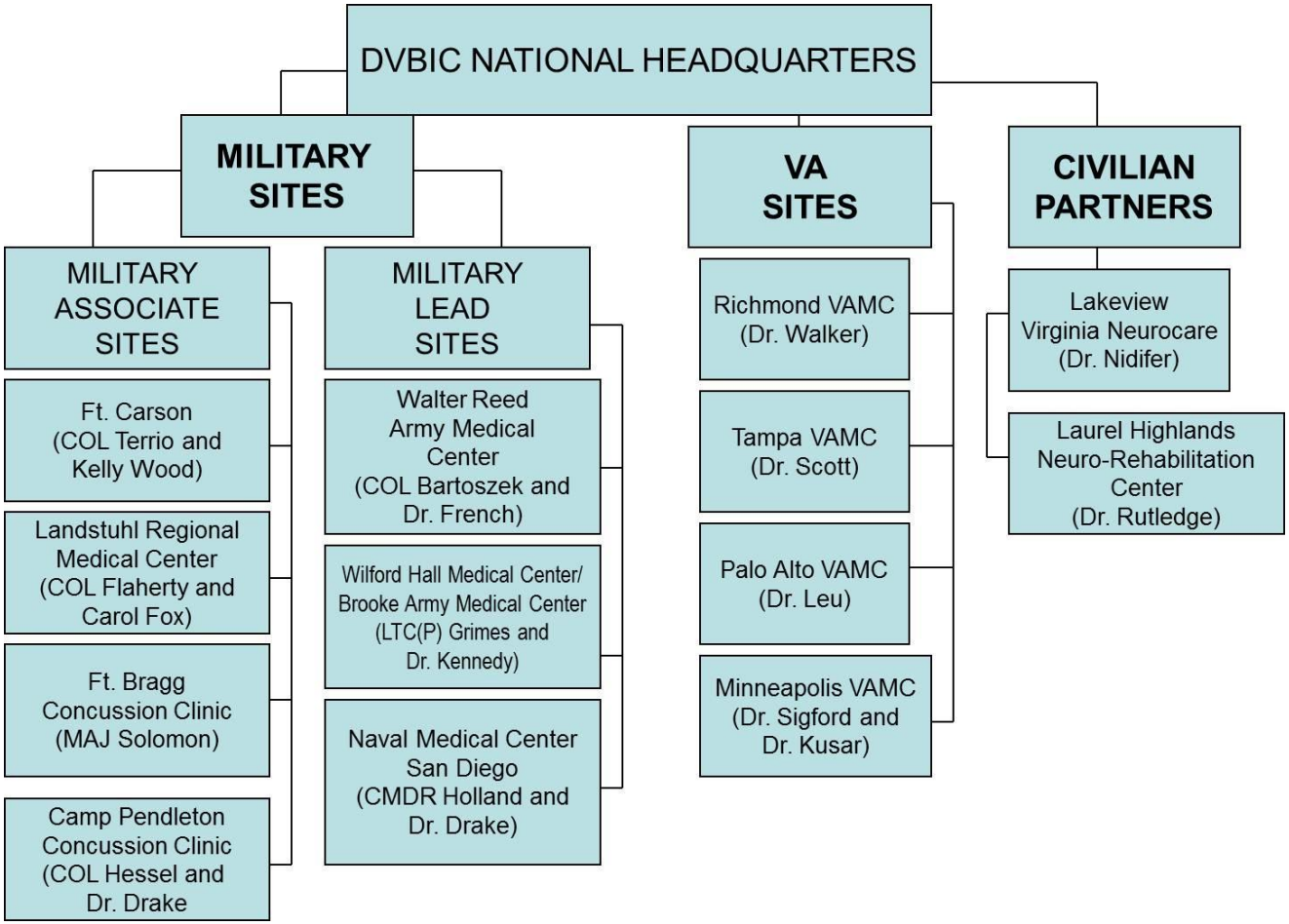
Mission Statement:

To determine and support best care practices for individuals with TBI through clinical, research, and education initiatives while providing a disease management system in DoD / VA

Location of DVBIC Sites



DVBIC Organization



DVBIC Subject Matter Expertise

- Defense Science Board (DSB) Taskforce on IED Threats and Mitigation
- CDC TBI Prevention Advisory Panel
- NIH TBI Classification Workshop Advisory Panel
- Interagency Committee on Disability Research
- Helmet Mounted Sensor Program
- Ad Hoc Reviews: MRMC, TATRC, Health Affairs, Congressional Offices

TBI Distribution by Service

TBI Patient Demographics: Service Branch

(n=5,926)

Service Branch	Number of Patients	Percentage of Patients
Army: Active Duty	3652	62%
Army: Reserve	203	3%
Army: National Guard	672	11%
Marine Corps: Active Duty	995	17%
Marine Corps: Reserve	73	1%
Air Force: Active Duty	90	2%
Air Force: Reserve	2	-
Navy: Active Duty	124	2%
Navy: Reserve	25	<1%
CIV/NATO	89	2%
Missing	1	-
Total	*5926*	

Source: Defense and Veteran Brain Injury Center (DVBIC) data current through February 29, 2008

What is the Incidence of Concussion/TBI in OIF/OEF Redeployers?

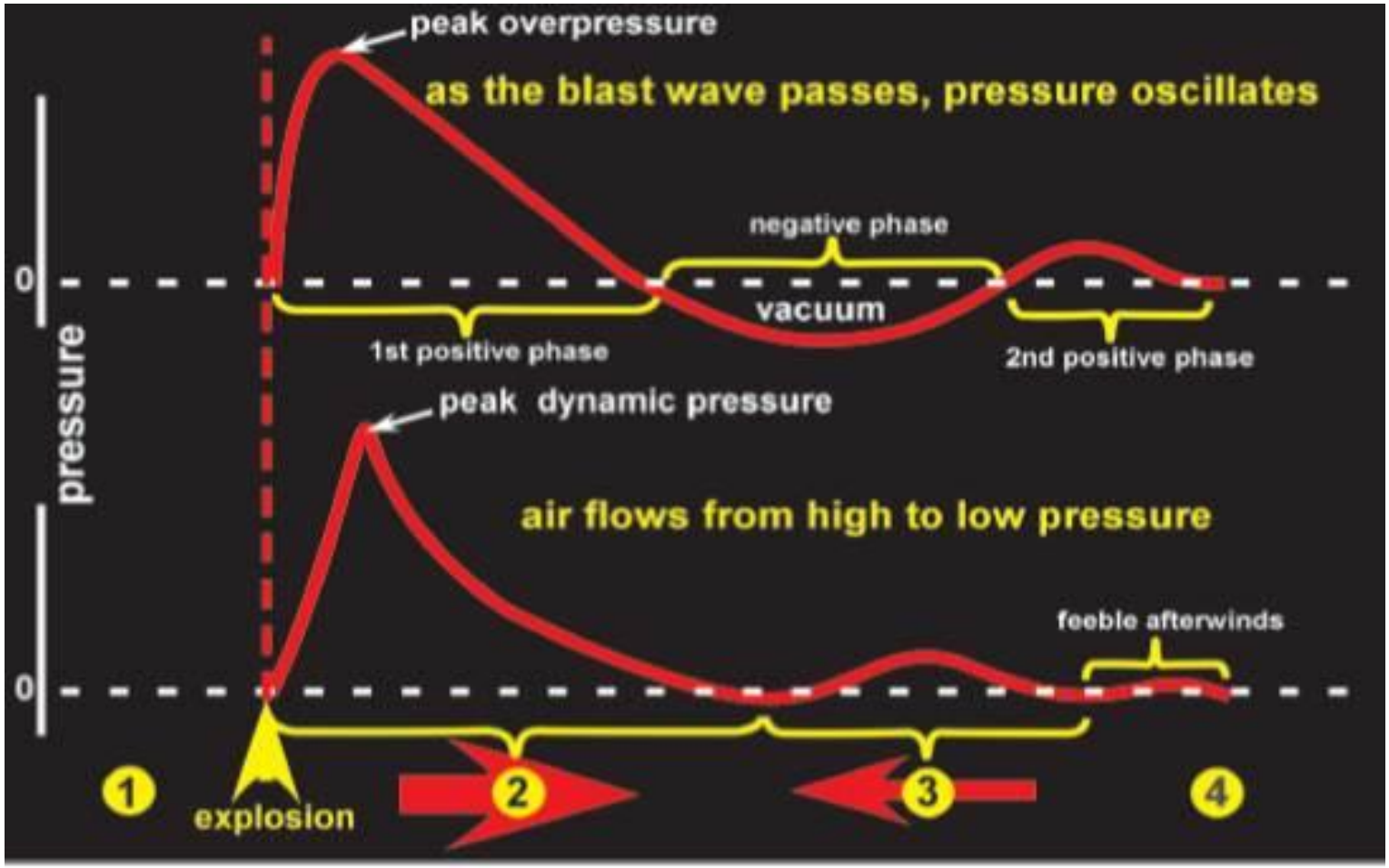
- Approximately 10-20% Screen +
  - Extrapolated from Post-Deployment Surveys
    - Camp Pendleton, 1 MEF, Ft Bragg, Ft Carson
  - Of these, ~50% have resolved with no current symptoms
  - Screen Does Not Equal Diagnosis

- VA Screen: 20% Screen +
  - Chart Review on 150 charts → Post-Concussive Dx in 3-6%

Incidence of Concussion in Theater

- MHAT-V added TBI questions
  - 11.2% of OIF SMs endorsed concussion/mTBI
  - Consistent with prior post-deployment surveys
- Concussion/mTBI Screening now added to PDHA for all Services
  - As of 1 April 2008

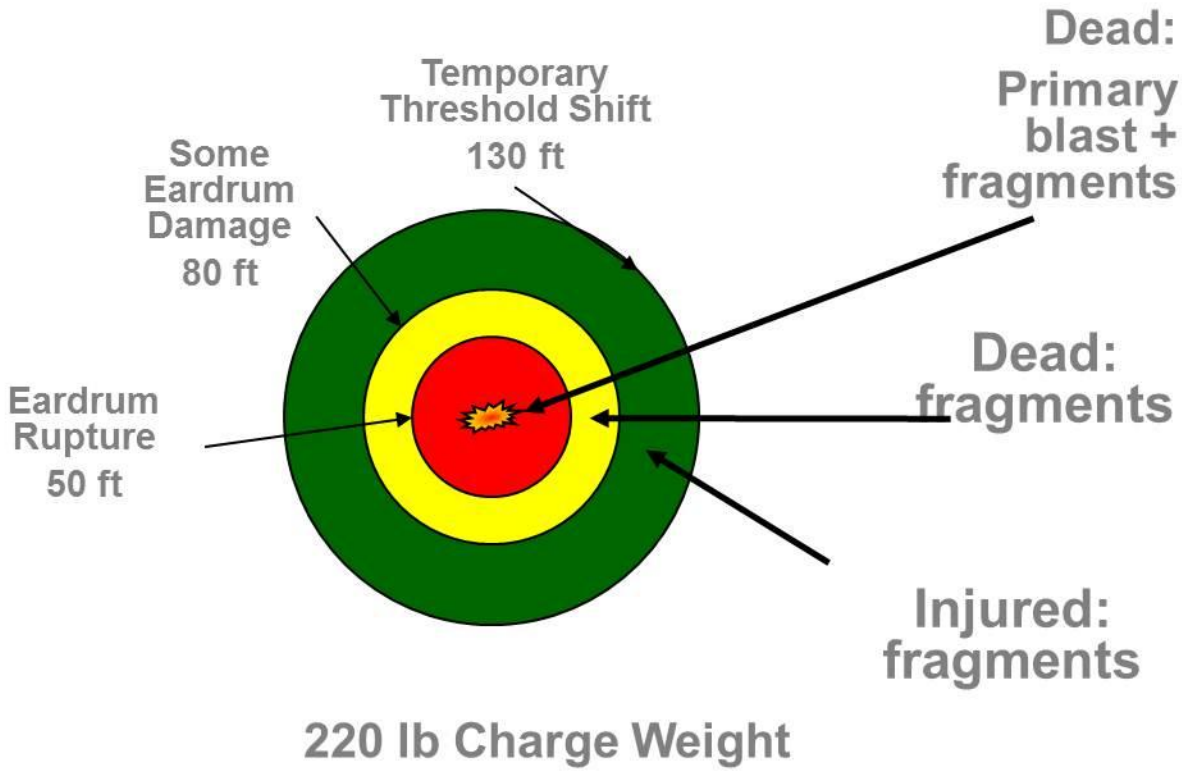
Overpressure/ Underpressure



Theories of Blast

- Overpressure / Underpressure Wave
  - Barotrauma
  - Debated: How Does Wave Transmit to Brain?
    - Vascular Hypothesis (Cernak, et al.)
    - Direct Hypothesis (Through Skull, Eyes and Ears)
- Air Embolism
- Development of Cavitation
- Development of Blast EM Fields

Open Space Explosions
Frame of Reference Debate



Primary Blast Effects: Animal Data

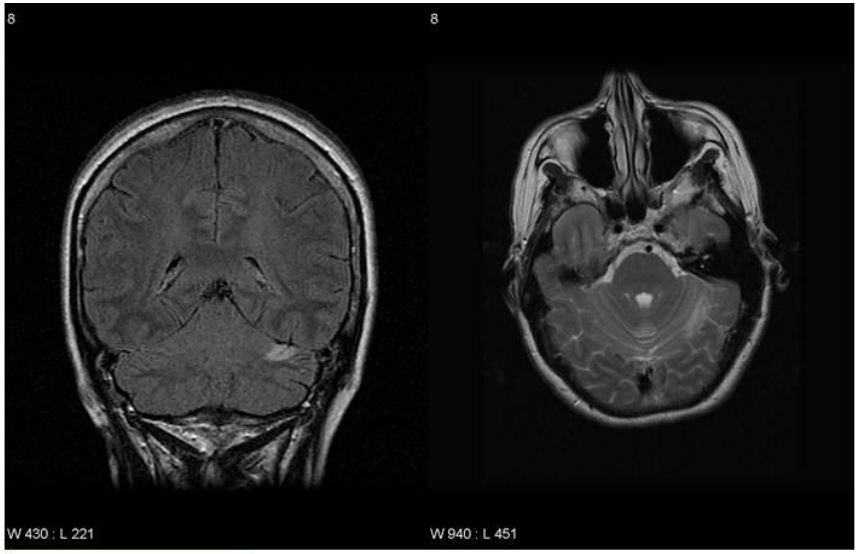
- Evidence from Animal Studies
  - Shock Tube
  - Detonation/Deflagration
- Neuropathology
  - Axonopathy
  - Edema, Hypertrophic Astrogliosis
  - Alteration in gene expression of iNOS (inducible nitric oxide synthetase)

Primary Blast Effects: Human Data?

- Most blast-associated combat TBI is multiple modality – “Blast +”
  - Acceleration-Deceleration (Humvee MVA)
  - Penetrating (associated shrapnel)

To date, one soldier with paraclinical evidence of primary blast without other modality

Primary Blast Injury



Blast Questions

- Is pathophysiology actually different?
- Since most injuries are “Blast +”, are we comparing 2 or more injuries to single-injuries?
- Is natural history of recovery different?
- Is there a different pattern of co-morbidity?

Cumulative Effects of Repeat Cerebral Concussion

- History of 3 previous concussions increases the risk of repeat concussions 3-fold. (Guskiewicz, 2003)
- Athletes with a hx of 3+ concussions report significantly more symptoms and have lower memory scores at baseline
- Symptoms following repeat concussion may be more serious and resolve at a slower rate.
- Worse case = “Second-impact syndrome”

Assess for prior exposures, follow more closely and expect more symptoms and slower recovery

Current Policy Controversies

- Definition / Nomenclature:
  - DoD Definition based on ACRM
  - LOC Only or ACRM Definition Using Both AOC and LOC?
  - ICD Coding
- Post-Deployment Screening
  - PDHA / PDHRA
  - Risks of Screening → Iatrogenic Harm?
- Psychiatric Sx: Co-Morbidity vs. Differential Dx
- Neurocognitive Testing
  - Utility of Baselining
  - Utility of Testing Post-Injury
  - CONOPS Plan for Theater
  - Role in Post-deployment

Definition Challenge

- Linking clinical phenomena (consciousness change) to physiological event (metabolic cascade)

- Loss of Consciousness
- Alteration of Consciousness

Neurometabolic cascade

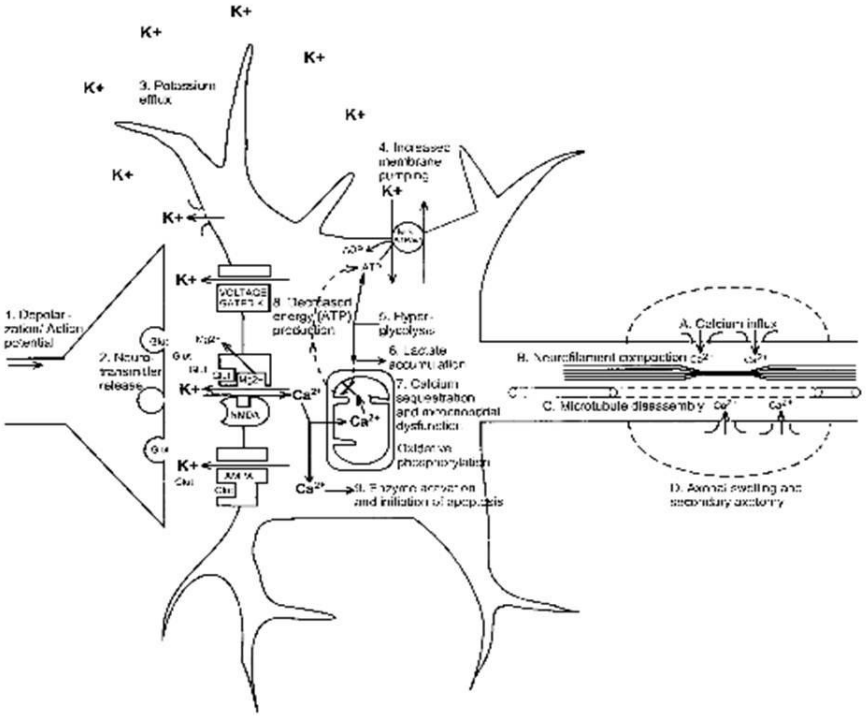
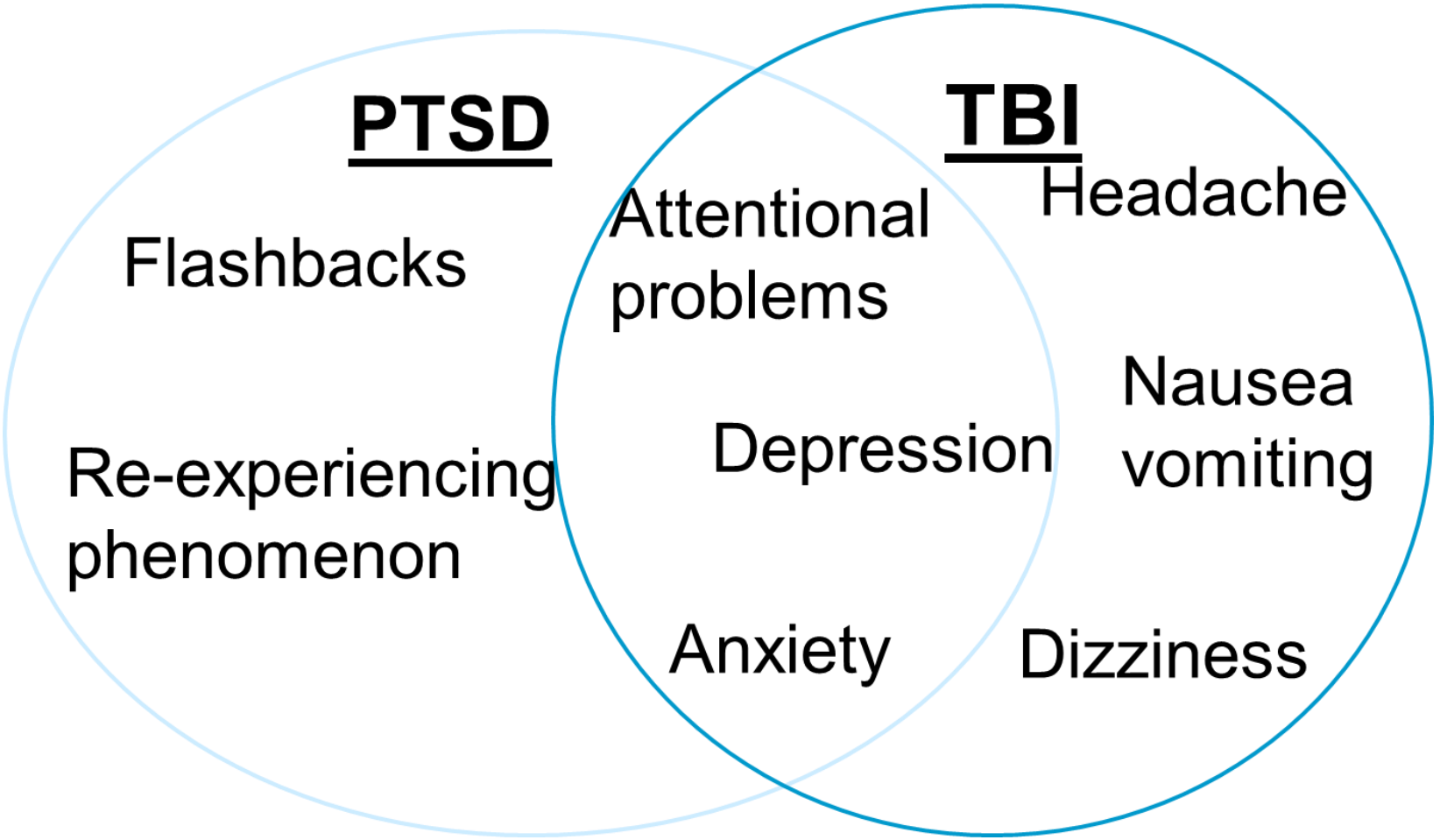


Figure 2. Neurometabolic cascade following traumatic injury. (1) Nonspecific depolarization and initiation of action potentials. (2) Release of excitatory neurotransmitters (EAAs). (3) Massive efflux of potassium. (4) Increased activity of membrane ionic pumps to restore homeostasis. (5) Hyperglycolysis to generate more adenosine triphosphate (ATP). (6) Lactate accumulation. (7) Calcium influx and sequestration in mitochondria leading to impaired oxidative metabolism. (8) Decreased energy (ATP) production. (9) Calpain activation and initiation of apoptosis. A, Axolemmal disruption and calcium influx. B, Neurofilament compaction via phosphorylation or sidearm cleavage. C, Microtubule disassembly and accumulation of axonally transported organelles. D, Axonal swelling and eventual axotomy. K^+, potassium; Na^+, sodium; Glut, glutamate; Mg^{2+}, magnesium; Ca^{2+}, calcium; NMDA, N-methyl-D-aspartate; AMPA, d-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid.

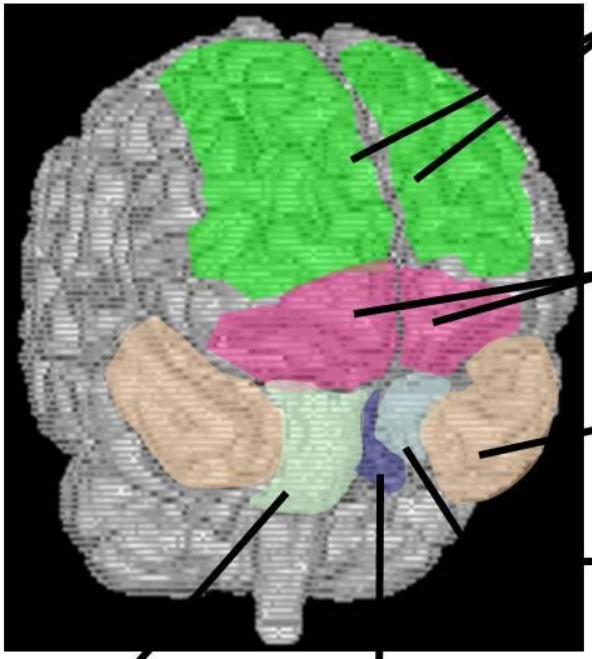
Giza et al. 2001

Clinicians Must Consider Both Dx



Brain Behavior Relationships and Regional Cortical Vulnerability to TBI

(Figure adapted from Arciniegas and Beresford 2001)



Dorsolateral prefrontal cortex
(executive function, including sustained and complex attention, memory retrieval, abstraction, judgement, insight, problem solving)

Orbitofrontal cortex
(emotional and social responding)

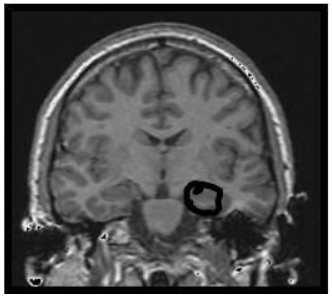
Anterior temporal cortex
(memory retrieval, sensory-limbic integration)

Amygdala (emotional learning and conditioning, including fear/anxiety)

Ventral brainstem
(arousal, ascending activation of diencephalic, subcortical, and cortical structures)

Hippocampal-Entorhinal Complex (declarative memory)

Viewed on coronal MRI →



Neurocog Testing Guidance

- **Armed Forces Epidemiological Board (Aug 06)**

  "At a minimum, implementing baseline [neuropsychological] testing should be considered pre-deployment and in military occupations at high risk for blast or impact injury."

- **TBI Task Force Report (May 07)**

  "Implement a baseline (pre-deployment), post-deployment, and post-injury/exposure neuropsychological evaluation using the ANAM. Utilize ANAM for neuropsychological testing per Acute In-Theater Care CPGs."

Neurocog Testing Guidance

- **DoD Independent Review Group (Apr 07)**
  - "Functional/cognitive measurements and screening should be developed and implemented upon entry and post-deployment health assessment to include the implementation of training for interpreters of screening and cognitive remediation for service members."
- **OSD/HA Scientific Advisory Panel (Oct 07)**
  - Supports use of ANAM with provisos; should be administered within 6 months of deployment; best employed at Echelons 2 and 3
- **NDAA 2008 HR 4986 (Jan 08)**
  - Section 1618 "ASSESSMENT.—The development and deployment of evidence-based means of assessing traumatic brain injury, posttraumatic stress disorder, and other mental health conditions in members of the Armed Forces, including a system of pre-deployment and post-deployment screenings of cognitive ability in members for the detection of cognitive impairment."

Cognitive Assessments

- Current OSD/HA to use ANAM for predeployment baseline in spiral approach
  - Free to DoD
  - Military Norms Available
- Head-to-Head Study of 5 instruments
  - National Academy of Neuropsychology appointed advisory panel
- OSD/HA Analysis of Alternatives
  - Focusing on IT/Systems Issues

Purposes of DHB TBI External Advisory Subcommittee

- Assist DHB in TBI Policy Recommendations to DoD
- Advisory Panel to DVBIC and DCOE

Committee Members

The Defense Health Board
Traumatic Brain Injury External Advisory Subcommittee

- Ross Bullock, Professor, Neurosurgery and Director, Neurotrauma Care, University of Miami
- Bob Cantu, Neurosurgeon, Chairman, Dept. Surgery, Emerson Hospital
- Guy Clifton, Professor and Chairman, Dept. of Neurosurgery, University of Texas Health Science Center
- Dave Hovda, Director of Brain Injury Research, Division of Neurosurgery, UCLA School of Medicine
- Grant Iverson, Professor, Faculty of Medicine, Dept. of Psychiatry, British Columbia Mental Health & Addiction Services
- James P. Kelly, Professor of Neurosurgery and Physical Medicine & Rehab, University of Colorado School of Medicine
- Jean Langlois, Senior Epidemiologist, Center for Disease Control
- Michael McCrea, Executive Director, Neuroscience Center, Waukesha Memorial Hospital
- William Perry, Professor of Psychiatry and President, National Academy of Neuropsychology, University of California
- Alan Ropper, Dept. of Neurology Brigham and Women's Hospital, Harvard Medical School
- William Snider, Professor of Neurology and Cell and Molecular Physiology, UNC Neuroscience Center
- Gale Whiteneck, Director of Research, Craig Hospital, Englewood, Colorado

Organizational Meeting

- 16 April 2008
- Paperwork, Ethics Brief, DHB Brief
- Briefings on DCOE and DVBIC
- Briefings on TBI Issues and Controversies in DoD
- Initial Planning/Brainstorming
- Chairman Selected:
  - Dr. James Kelly

Initial Issues Identified by Subcommittee

- Assessment and Management Issues Related to RTD
  - Neurocognitive Assessment
- Screening Issues
  - Benefits vs. Potential Iatrogenic Risks
  - Evaluation of Available Data

Initial Issues Identified by Subcommittee

- Prevention Measures
  - Detector/Dosimeter Technology
  - Helmet Design
- Scientific Priorities / Gap Identification
  - Requested Review of CDMRP Process and Results
- Delivery Systems
  - Availability of Resources

Future Meetings

- Goal: 6 meetings/year
- Combination of Telephone and In-Person
- Next Meeting: June 2008