Rehabilitation in Traumatic Brain Injury

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Combat Casualty Care Research Program
and Joint Program Committee 6 (CCC)
US Army Medical Research and Materiel Command
January 15, 2013

The views expressed in this presentation are those of the author and do not reflect official policy or position of the Department of the Army, Department of Defense or the U.S. Government. I have no relevant financial relationships to disclose.
IN THE LAB, ON THE BATTLEFIELD

USAMRMC Mission and Vision

MISSION

Provide medical knowledge and materiel lifecycle management to protect, treat and optimize warfighter health and performance across the full spectrum of operations.

VISION

We are the world’s experts and leaders in the military relevant biomedical research and medical materiel communities, delivering the best medical solutions to enhance, protect, treat, and heal our warfighters.
Military vs. Civilian Biomedical R&D

<table>
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<tr>
<th>Area</th>
<th>Civilian Focus</th>
<th>USAMRMC Focus</th>
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<td>General</td>
<td>• Maintaining health</td>
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<td>Drivers</td>
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<td>• Market forces</td>
<td>• Operational expediencies</td>
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<td>Trauma</td>
<td>• Septic shock</td>
<td>• Penetrating trauma and hemorrhagic shock</td>
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<td></td>
<td>• Hospital-based care by physicians</td>
<td>• Field care by self, buddy or medic</td>
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<td></td>
<td>• Rehabilitation</td>
<td>• Reducing medical logistics</td>
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<td>Infectious Disease</td>
<td>• Diseases endemic in CONUS</td>
<td>• Diseases endemic in OCONUS</td>
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<td></td>
<td>• Global pandemics</td>
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<td>Operational</td>
<td>• Industrial occupational environments</td>
<td>• Extreme physical environments and workloads</td>
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<tr>
<td>Medicine</td>
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<tr>
<td>MCBDP</td>
<td>• Post exposure treatment</td>
<td>• Pre-exposure protection</td>
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<td></td>
<td>• Detect to treat</td>
<td>• Emerging threats</td>
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<td>• Diagnostics</td>
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IN THE LAB, ON THE BATTLEFIELD
Joint Program Committees Managing TBI Research

- JPC 5 – Military and Operational Medicine
  - mTBI with PTSD and mTBI with other co-morbidities
  - Prevention, protection
  - Cognitive readiness and rehabilitation
- JPC 6 – Combat Casualty Care
  - Management of spectrum of TBI
  - Point of injury to initial weeks in US Facility
- JPC 8 – Clinical and Rehab Medicine
  - US Military Treatment Facilities
  - Until returned to duty, medically boarded and/or transferred to VA care
Defense Medical Research and Development Program

Defense Medical Research and Development Program Process

SecDef Direction + JFHP CONOPS JCDs → Capability Gap Assessment

USAMRMC Program Management Support

- Medical Training and Health Information Sciences
- Infectious Diseases
- Operational Medicine
- Combat Casualty Care
- Radiation Health Effects
- Clinical & Rehabilitative Medicine

Joint Program Committees (JPCs) → MHS Strategic Imperatives

R&D Opportunities (PA/RFI/RFP)

- Scientific Peer Review of Research Proposals
- Program Review of Research Proposals

Execution Agents
- USAMRMC
- USUHS
- ONR
- AFOSR
- BUMED
- AFSG
- Academia/Industry/Govt

USAMRMC = US Army Medical Research and Development Command; USUHS = Uniformed Services University; ONR = Office of Naval Research; AFOSR = Air Force Office of Scientific Research; BUMED = Navy Bureau of Medicine and Surgery; AFSG = Air Force Surgeon Generals Office

JFHP CONOPS = Joint Force Health Protection Concept of Operations; JCD = Joint Capabilities Document

MHS = Military Healthcare System

PA = Program Announcement

RFI = Request for Information

RFP = Request for Proposals

IN THE LAB, ON THE BATTLEFIELD
DoD Joint Program Committee
Strategic Research Planning Process


Resource Allocation (DHP, Army, SBIR)

Strategic Planning

Program Announcements/Requests for Proposals/Broad Agency Announcement

Research Prioritization

Resource Prioritization Factors (Portfolio Balance, Political, Intramural Lab Capabilities, etc.)

Implementation Plan

Implementation Barriers Analysis (Manpower, Federal Acquisitions Regulation, Budget Related, Size of Portfolio)

Review and Analysis (Army, Navy, Air Force, Marines, VA, ASD/HA, NIH, NIMH, Academic Subject Matter Experts)

Portfolio Analysis
- Create database
- Analyze Intramural and Extramural Investments
- Identify Areas for Resolution
- Identify Findings for Transition

Transition of select Materiel Solutions to Advanced Development

Dissemination of knowledge/ Clinical Practice Guidelines
Mission

To reduce the impact of injury and overall death rate resulting from battlefield wounds

Meet Demands on First Responders
- Patient monitoring/assessment technologies
- Decision-assist algorithms/devices

Reduce the Number of Deaths on the Battlefield
- Damage control resuscitation
  - Clotting factors (TXA, fibrinogen, etc.)
  - Dried plasma, other blood products
  - Bleeding control devices/bandages
- Enhanced resuscitation fluids

Limit Brain Damage
- Biomarkers
- Screening & Diagnostic devices
- Neuroprotective drugs
- Neuroplasticity

Definitive Care of Combat Injuries
- Improved definitive care for orthopedic and maxillofacial injuries
- Improved wound/burn care
- Improved vascular surgery
- Treatments for lung injury due to smoke & blast

Clinical Trials
- Test advanced therapies and devices for use in Role 1 through early Role 4

Improve En Route Care
- Oxygen conservation
- Closed loop algorithms
- Lightweight modules
- “Virtual ICU”

Reduce Morbidity and ‘Died of Wounds’ Rate
- Full physiologic life support
- Reduce complications from blood loss
- Maintain tissue viability
IN THE LAB, ON THE BATTLEFIELD

Combat Casualty Care Key Focus Areas

- **Mortality**
  - Non-compressible Hemorrhage
    - Including Coagulopathy
    - Compressible Hemorrhage
      - Extremity
      - Axilla/neck/groin
    - Pneumothorax
    - Airway Compromise
    - Multisystem Organ Failure
    - Sepsis *(w/ JPC2)*
    - Deep Vein Thrombosis
    - Other
  - Compressible Hemorrhage
  - Extremity
  - Axilla/neck/groin

- **Morbidity**
  - Traumatic Brain Injury
    - Mild *(w/ JPC5)* to Severe
    - Massive Soft Tissue Injury
    - Orthopedic Trauma
      - Spine trauma
      - Spinal Cord Injury
      - Complex extremity *(w/ JPC8)*
    - Burn
    - Craniofacial Injury
    - Pain (acute and chronic)
  - Training *(w/ JPC1)*
    - Medic
    - Specialty Surgeon
    - Other Providers

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IN THE LAB, ON THE BATTLEFIELD

Co-Morbidities Associated with mTBI and PTSD

- Sleep disorders
- Substance abuse
- Psychiatric illness
- Vestibular disorders
- Visual disorders
- Cognitive disorders


Traumatic Brain Injury

- 52,000 Deaths
- 275,000 Hospitalizations
- 1,365,000 Emergency Department Visits

??? Receiving Other Medical Care or No Care*

Chronic Pain
N=277
81.5%

PTSD
N=232
68.2%

TBI
N=227
66.8%

16.5%
2.9%
42.1%

10.3%
12.6%
6.8%

5.3%

http://www.cdc.gov/traumaticbraininjury/statistics.html
Accessed 22 Feb 2012
## DoD-VA TBI definition and TBI threat

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
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<tbody>
<tr>
<td>Normal Structural Imaging</td>
<td>Normal or abnormal structural imagining</td>
<td>Normal or abnormal structural imagining</td>
</tr>
<tr>
<td>LOC = 0 – 30 minutes</td>
<td>LOC &gt; 30 minutes and &lt; 24 hours</td>
<td>LOC &gt; 24 hours</td>
</tr>
<tr>
<td>AOC = a moment up to 24 hours</td>
<td>AOC &gt; 24 hours Severity based on other criteria</td>
<td>AOC &gt; 24 hours Severity based on other criteria</td>
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<tr>
<td>PTA = 0 – 1 day</td>
<td>PTA &gt; 1 day and &lt; 7 days</td>
<td>PTA &gt; 7 days</td>
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<tr>
<td>GCS = 13 – 15</td>
<td>GCS = 9 – 12</td>
<td>GCS = 3 – 8</td>
</tr>
</tbody>
</table>

LOC = loss of consciousness, AOC = alteration of consciousness/mental state, PTA = post-traumatic amnesia, GCS = Glasgow Coma Scale

### TBI Diagnoses in U.S. Armed Forces

- **2000**: 10,963
- **2001**: 11,830
- **2002**: 12,470
- **2003**: 12,898
- **2004**: 13,312
- **2005**: 12,211
- **2006**: 16,958
- **2007**: 23,174
- **2008**: 29,255
- **2009**\*: 31,407
- **2010**: 30,380

*2000-2009 annual numbers updated as of 16 May 2011

**2010 – 2011 annual numbers updated as of 10 Feb 2012**
Joint Integrated Research Approach

1. Basic Training DoD-DHP
2. Mobilization DoD-DHP
3. Deployment DoD-DHP
4. Employment DoD-DHP
5. Re-Deployment DoD-DHP
6. Post-Deployment DoD-DHP
7. Reset

DEVELOPING AND MAINTAINING A FIT AND READY FORCE

Treat Casualties DoD/NIH/VA
Reconstitution DoD-DHP
K-12 thru Accession NIH/ED
Readiness DoD-DHP
Separation DoD/VA
Post-Military Surveillance DoD/NIH/VA/ED

Deployment DoD-DHP
Post-Degement DoD-DHP
Deployment DoD-DHP
Reconstitution DoD-DHP
Reset

IN THE LAB, ON THE BATTLEFIELD

Continuum of TBI Care Determines Research Approach

RESEARCH NEEDS

**Injury Prevention**
- Medical Standards for Protective Equipment

**RDT&E:**
- Combat Casualty Care
  - Objective Measure of Head Impact/Blast Exposure
  - Valid Criteria & Objective Servicemembers/Concussion Screening Tool
  - Portable Fieldable Diagnostic Device (In Theatre & Garrison)

**Psych Health and Related Symptoms**
- Pharmaceuticals & Surgical Technology
- Recovery Timecourse & Rehabilitation
- Valid RTD Standards & Measures of Rehabilitation

**Return to Duty/Disability/Reclassification Assessment**
- Continuing Education and Reinforcement for Servicemembers, Leaders and Service Providers

<table>
<thead>
<tr>
<th>1. Basic Science &amp; Epidemiology</th>
<th>2. TBI/Concussion Prevention/Education &amp; Training</th>
<th>3. Possible TBI/Concussion from Impact or Blast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutraceuticals, Standards for Helmets, Education/CPG’s for Servicemembers, Leaders &amp; Service Providers</td>
<td>Portable Fieldable Diagnostic Device (In Theatre &amp; Garrison)</td>
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<td>Head Impact/Blast Injury Dosimeter (Fielding HMSS Gen 2 &amp; DARPA Blast Gauge 2012)</td>
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**Solutions**

Injury Prevention
- Medical Standards for Protective Equipment

RDT&E:
- Combat Casualty Care
  - Objective Measure of Head Impact/Blast Exposure
  - Valid Criteria & Objective Servicemembers/Concussion Screening Tool
  - Portable Fieldable Diagnostic Device (In Theatre & Garrison)

Psych Health and Related Symptoms
- Pharmaceuticals & Surgical Technology
- Recovery Timecourse & Rehabilitation
- Valid RTD Standards & Measures of Rehabilitation

Return to Duty/Disability/Reclassification Assessment
- Continuing Education and Reinforcement for Servicemembers, Leaders and Service Providers

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Neuropathology studies of military TBI (Perl/USU)
Current Assessment of mTBI/Concussion Research

- Lack of a validated case definition of mTBI (still)
  - 41 definitions/guidelines identified by WHO (J Rehabil Med. 2005 May;37(3):137-41)
  - Recent review by DoD-funded working group to develop concussion definition guidelines found that only 0.5% of literature identified was of MEDIUM quality and had inclusive case definitions and reported data at fixed time points relevant to one or more of the key questions they sought to address.

- TBI is heterogeneous-saying that one has experienced a “mild TBI” is akin to saying one has experienced a “motor vehicle collision” – it is a category error (J Trauma Acute Care Surg. 2012;73: S13YS23.)

- High frequency of exposure to blast related impact and non-impact (multiple exposures per warfighter)

- Co-morbidity with other Soldier behavioral health concerns (e.g. PTSD, depression, anxiety, suicidality, alcohol and drug abuse, risk taking behaviors, etc.)

- Multiple factors may complicate recovery from mTBI for soldiers wounded in theater (Hoge, CW et al. Mild traumatic brain injury in US soldiers returning from Iraq. NEJM 2008; 358)
  - Risk of repeated head injuries
  - Misdiagnosis or under diagnosis
BTF & CDC Partnership with Alliance Partners for Concussion Definition Guidelines

PI: Jamshid Ghajar  Org: Brain Trauma Foundation, Centers for Disease Control

Study/Product Aim(s)

• Assemble a multi-disciplinary team of topic experts, bio-informaticians, methodologists, and dissemination/implementation experts.
• Conduct a systematic review and rigorous quality assessment of the literature in order to provide the multi-disciplinary team with the evidence to support the definition process.
• Craft a functional definition for concussion.
• Employ a comprehensive process to ensure maximum dissemination and implementation of the definition, and to evaluate the success of that process.

Approach

To provide a clear definition guideline that will enable clinicians, field medics, researchers, and athletic supervisors to address questions of screening, identification, diagnosis, prognosis, and treatment.

Goals/Milestones

FY 11 Goals-
☑ Assemble a task force which will train in the systematic processes with specific tasks
☐ Search, assess, and summarize literature
☐ Articulate Key questions along with scope and parameters of project.

FY 12 Goals-
☐ Data analyses
☐ Finish preparing data set, transfer to Westat for analyses
☐ Disseminate

FY 13 Goals-
☐ Create a final report on partnership outreach efforts and implementation activities.

Comments/Challenges/Issues/Concerns  None currently

Timeline and Cost

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<tr>
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<th>FY 11</th>
<th>FY 12</th>
<th>FY 13</th>
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<td>Phase 1 – Initiation</td>
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<td>Phase 2 – Surveillance</td>
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<td>Phase 3 – Specification</td>
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<td>Phase 4 – Definition</td>
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<td>Phase 5 – Dissemination</td>
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Updated: (20 DEC 12)
Six Ways to the Same GCS

FIG. 1. Heterogeneity of severe traumatic brain injury (TBI). Computed tomography (CT) scans of six different patients with severe TBI, defined as a Glasgow Coma Scale score of <8, highlighting the significant heterogeneity of pathological findings. CT scans represent patients with epidural hematomas (EDH), contusions and parenchymal hematomas (Contusion/Hematoma), diffuse axonal injury (DAI), subdural hematoma (SDH), subarachnoid hemorrhage and intraventricular hemorrhage (SAH/IVH), and diffuse brain swelling (Diffuse Swelling).

Current Assessment of Mild thru Severe Research

- Blast and impact TBI models require standardization
- Mild and repetitive mild TBI models require validation
- Blast effects may have a unique signature of injury, but it is very difficult to isolate primary blast wave components from rotational acceleration
- Screening/Assessment development has shown promise
  - Serum Biomarkers
  - Physiologic Assessments (quant EEG, Smooth Pursuit Eye Tracking, etc)
  - Imaging (Diffusion Tensor, High Definition Fiber Tractography, Positron Emission Tomography, functional MRI, MR Spectroscopy, etc)
  - Neuropsychological Assessment Tests (NPATs)
- While many therapies have appeared useful in pre-clinical models, they have not successfully translated to clinical use
  - Developed Federal Interagency TBI Research Informatics System with NINDS
  - Evaluating international comparative effectiveness research effort that in turn may help refine pre-clinical models
  - It may well be that past trials have failed simply because we do not have the capability to properly measure the effect of a given therapy in humans
Drug Target Mechanisms

IN THE LAB, ON THE BATTLEFIELD

Inflammation

Drug Target Mechanisms

Min     Hr                  Days                                  Weeks                                                   Months

Injury

Excitotoxic damage

Oxidative stress

Necrosis

Axonal injury

Apoptosis

Demyelination

Microgliosis

Neuroregeneration

 Diseases

[Protein Biomarker] blood

Supplemental Nutrition/Oxygen

- Omegaven
- Omega 3
- Hyperbaric Oxygen
- Oxycyte
- Perfluorocarbons (Perftec, Oxycite, Oxygent)

Other or Uncertain Mechanism

- Galantamine
- Methylphenidate
- Simvastatin, Atorvastatin

Stem Cell Therapy
Federal Interagency TBI Research

A collaboration between NIH and DOD to develop a biomedical informatics system to accelerate scientific discovery and treatment in Traumatic Brain Injury.

Database with multiple contributors and multiple accessors
Common Data Elements

Streamline Your Neuroscience Clinical Research using these content standards that enable clinical investigators to systematically collect, analyze, and share data across the research community. The NINDS strongly encourages researchers who receive funding from the Institute to ensure their data collection is compatible with the common data elements (CDEs).

CDEs now available:
- General (CDEs that cross diseases)
- Epilepsy
- Spinal Cord Injury
- Traumatic Brain Injury

CDEs in development:
- Stroke - Public comments under review
- Parkinson’s Disease - Final development
- Frontotemporal Dementia
- Huntington’s Disease
- Amyotrophic Lateral Sclerosis
- Neuromuscular Disease
  - Congenital Muscular Dystrophy
  - Friedreich’s Ataxia
- Headache

Investigators and Research Teams – launch studies with CDEs: The CDE Standards
Data Managers and Programmers – incorporate the CDEs into your systems: Use
Discover how the CDE Project collaborates with others: Learn more about the

http://www.commondataelements.ninds.nih.gov/
Rehabilitation after TBI

- Much of what is used was developed in the stroke and SCI rehab arenas
  - Stroke is a focal, relatively homogeneous injury, TBI often diffuse
  - Providers tend to use what they were taught
  - Many approaches are un- or poorly validated (our Servicemembers deserve Evidence-Based approaches)
  - Definition of “recovered” is problematic especially for mTBI
    - Do we truly recover?
  - Outcome assessments are also a challenge
    - Many different assessments
    - Some can have coarse granularity (e.g. Glasgow Outcome Scale-Extended)
Rehabilitation after TBI

- **Assistive Technologies**
  - Cueing/reminder systems
  - Touch screens
  - Assistive animals
  - Speech synthesizers
  - Special eyewear (prisms, patches, etc)

- **Rehabilitation Technologies**
  - Plasticity (nearly all can leverage computer-based/simulation/virtual reality technologies)
    - Physical Therapy (repetition)
    - Speech Therapy (swallowing)
    - Occupational Therapy
    - Vision Therapy
  - Neuromodulation
    - Cranial Nerve Stimulation (non-invasive and invasive)
    - Deep Brain Stimulation (invasive)
Cranial Nerve Non-Invasive Neuromodulation

**PI:** Dr Brett Logan, Blanchfield Army Community Hospital, Ft Campbell  **Consultant:** Dr Yuri Danilov, TCNL, U. Wisc-Madison

### Background

- CN-NINM has been demonstrated to create localized functional changes in brain activity levels, resulting in improved balance, posture, gait and limb movement control.

### Approach

- The daily training regimen during the initial 2-week intensive phase will consist of two 90-minute 1-on-1 sessions with the trainer each day. Sessions comprised of 3 elements:
  - **20-Minute Movement Training** (with PoNS™) Targeted training of body segments that typically move in synergistic adaptive patterns teaches the subject to develop isolated muscle control, joint mobility, relaxation, and strength. The goal of this training is to improve body awareness and re-train movements for improved neuromuscular control and mobility.
  - **20 Minute Balance Training** (with PoNS™) The goal of balance training is to create body awareness, correct postural alignment, and improve balance by recalibrating proprioceptive, tactile and vestibular inputs. Initial balance training requires that the subject perform three progressively challenging 5-minute balance trials while using the PoNS™ device. The dimensions of the base of support and compliance of the seated or standing surface (sensory conditions) are varied to advance the challenge as appropriate.
  - **20-Minute Cognitive/Memory/Attention Training** (with PoNS™) will be performed using a customized software program employing the Brain Fitness™ (Posit Science, San Francisco, CA), the HighIQPro Braintraining suite, or equivalent. The ability to sustain mental effort in purposeful, goal-directed activity will be continually monitored, and the training program progressed to maintain engagement and aid recovery in the identified functional deficits.

### Analysis and Expected outcomes:

Both individual (n=1) and cohort data set analysis will be conducted to identify both specific and generalizable effects of the intervention methods. We predict small but important changes after the first week of the In-Clinic intervention, and then progressive improvements in these scores in the successive weeks both In-Clinic and after training at home. We anticipate that subjects will begin to observe meaningful behavioral changes in both balance and gait, which hopefully will serve as a catalyst for continued effort and concomitant progress in these areas. In the latter phase of the study we also expect to observe functional transfer to other activities of daily living that contribute to improved quality of life and consequent mental health benefits, although we will not be formally measuring these outcomes in this pilot study.

Cognitive/Motor Therapy Application Using Console-Based Videogame Platform (Blue Marble)
Flynn, Sheryl
Blue Marble Co.
OSD DHP SBIR 2009.1
1 Jul 2009 to 31 Oct 2014

<table>
<thead>
<tr>
<th>Aims</th>
<th>Deliverables</th>
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<tbody>
<tr>
<td>• Complete Phase I/II development of a cost-effective intervention that induces the brain plasticity necessary for return to duty and/or a fulfilling civilian life</td>
<td>• A low-cost, video game-based intervention tool to train cognitive and sensorimotor domains in preparation for a service member’s return to duty following mTBI</td>
</tr>
<tr>
<td><strong>Approach</strong></td>
<td><strong>Status</strong></td>
</tr>
<tr>
<td>• Continue Phase I development of prototype version of game and assess/compare with neuropsychological tests using participants with TBI and subject matter experts</td>
<td>• In Phase I, developed game storyboard and narrative, report on most appropriate technology for software version of game, the game design document, and basic interactive software demonstration of the core game mechanic</td>
</tr>
<tr>
<td>• Refine prototype as needed based on programming bugs/issues, visual issues, audio requirements, data storage, incorrect output, and enjoyment level and complete Alpha version</td>
<td>• Completed formal play-test of the rough prototype</td>
</tr>
<tr>
<td>Conduct an intervention with the alpha version of the game; provide participants with study packet including the game for download and detailed instructions</td>
<td>• Currently completing phase II and moving to phase II-plus where a validation study will be executed</td>
</tr>
<tr>
<td>Revise Alpha version and complete Beta 2 version of game</td>
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Using Real-Time Functional Imaging To Speed Recovery From TBI
PT100120, Department of Defense

PI: Drs. Gabrieli, Van Boven  Org: MIT, Geneva Foundation

**Study Aim(s)**
- Recruit 120 active service men and women with mTBI; 60 with and 60 without PTSD
- Characterize structural and functional brain patterns
- Assess the efficacy of real-time fMRI and/or computer-based cognitive training in reducing symptoms of mTBI
- Predict treatment response and outcomes for mTBI

**Approach**
The aim is to perform a randomized, double-blind clinical trial to determine the efficacy of realtime fmri training and/or cognitive training on improving executive function, memory, and attention of 120 soldiers diagnosed with a history of Mild Traumatic Brain Injury (mTBI) with or without comorbid PTSD. Every participant will undergo an 8-week training program with pre and post clinical, neuroimaging and behavioral assessment and four realtime fmri training sessions evenly spaced during the training.

**Timeline**

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<tr>
<td>Protocol setup/IRB approval</td>
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<td>Recruitment, data acquisition</td>
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<td>Data analysis</td>
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<td>Finalize analysis and publications</td>
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**Goals/Milestones**

**CY11 Goal** – Protocol refinement and IRB approval
- IRB approval
- Acquisition of neuropsychological battery

**CY12 Goals** – Instrumentation setup and data acquisition
- Create realtime fMRI setup for external use and image analysis workflow
- Register trial and begin recruitment and data acquisition

**CY13 Goal** – Acquisition and analysis
- Continued data acquisition and analysis

**CY14 Goals** – Acquisition, analysis, publication
- Finalize data analysis

**Comments/Challenges/Issues/Concerns**
- None at this time

Updated: Cambridge, MA 01/06/2013
Neural Markers and Rehabilitation of Executive Functioning in Veterans with TBI and PTSD

PI: Elbogen  
Org: University of North Carolina – Chapel Hill

Study/Product Aim(s)

The study involves a randomized clinical trial of an empirically-supported cognitive rehabilitation intervention that targets improved executive functioning, with the participation of N=100 veterans diagnosed with both TBI and PTSD (n=50 in experimental group and n=50 receiving usual care). The study aims to:

1. Use functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) to evaluate changes in neural circuitry and neural activity associated with executive function as a result of cognitive rehabilitation intervention.
2. Evaluate neurocognitive and behavioral changes associated with a cognitive rehabilitation interventions among veterans with TBI/PTSD.
3. Assess the impact of cognitive changes on irritability/impulsivity and social/occupational functioning among veterans.

Approach

Experimental participants will be instructed to practice iPod touch applications that have shown to improve inhibitory control and self-monitoring behavior and also include an application to randomly cue participants to practice executive functioning skills whereas control participants will be instructed to practice iPod touch applications on visual memory. Family members in both groups will be trained as “mentors” to reinforce veterans’ use of the applications in everyday living environments. Components of the intervention will be administered via an iPod touch interviews, neurocognitive testing, fMRIs, and EEGs will be conducted before and after the intervention period to evaluate the participant's functioning.

Goals/Milestones

FY11 Goal – Prepare for clinical trial
☐ Obtain study approval from UNC IRB and USAMRMC

FY12 Goals – Implement clinical trial
☐ Develop data collection system
☐ Train research personnel
☐ Begin recruitment, baseline data collection, and implementation of cognitive rehabilitation intervention

FY13 Goal – Communicate study progress/findings
☐ Begin follow-up data collection
☐ Present study progress at national conferences

FY14 Goals – Data analysis and production of deliverables
☐ Conduct statistical analysis
☐ Prepare manuscripts for publication

Comments/Challenges/Issues/Concerns

• We currently have no significant issues or concerns to report.

Timeline

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<td>Prepare for Clinical Trial</td>
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<td>Conduct Baseline/Follow-up Data Collection</td>
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<td>Implementation of Intervention</td>
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<td>Data analysis and manuscript preparation</td>
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Updated: (October 2012)
Enhanced Cognitive Rehabilitation to Treat Comorbid TBI and PTSD

PI: Amy Jak, Ph.D.  Org: Veterans Medical Research Foundation

Study Aim(s)

**Primary Aim 1:** To investigate the efficacy of SMART-CPT in reducing emotional and neurobehavioral symptom severity in veterans with comorbid TBI and PTSD.

**Primary Aim 2:** To investigate the extent of cognitive changes in veterans with comorbid PTSD and TBI following treatment with SMART-CPT.

Approach

Randomized controlled treatment study to test a modification of Cognitive Processing Therapy (CPT) for PTSD in which CPT is interweaved with compensatory cognitive rehabilitation principles (CogSMART) to create a hybrid treatment, SMART-CPT. The study will enroll 72 veterans diagnosed with both PTSD and a history of mild to moderate TBI and randomize half to receive standard CPT and half to receive SMART-CPT for 12 weekly sessions. Veterans will also receive comprehensive symptom, mental health, and neuropsychological assessments at 3 timepoints during the study. The investigation seeks to improve treatment outcomes for combat-related psychological health and develop an evidence-based intervention for treatment of comorbid TBI and PTSD.

Goals/Milestones

**FY12 Goal – Study Start Up**
- Regulatory approvals obtained
- Study staff hired/trained

**FY13 Goals – Recruitment, Enrollment, Treatment, and Assessment**
- Ongoing recruitment
- Assessment/Treatment protocol (8 in active treatment phase)

**FY14 Goal – Ongoing recruitment, treatment protocol, data entry**
- Ongoing recruitment/enrollment/treatment protocol
- Data entry

**FY15 Goals – Data Analysis, Presentation, Publication**
- Data Analysis
- Dissemination of Results

Comments/Challenges/Issues/Concerns

Study proceeding as planned

Updated: (October 31, 2012)
Study/Product Aim(s)
- Evaluate PACR’s efficacy in patients with persistent post-concussive symptoms (PPCS) following mild traumatic brain injury (mTBI, including blast exposure).
- Evaluate the effect of PACR on generalized cognitive and functional performance.
- Evaluate the endurance of effects following completion of PACR use.
- Identify specific populations of treatment responders and non-responders.

Approach
Team will employ a standard parallel arm, prospective, randomized, controlled, double-blind trial design of a treatment group using PACR vs. an active control group using computer games in 132 participants with PPCS following mTBI.

Sites: Walter Reed National Military Medical Center, Tripler Army Medical Center, Boston Veterans Administration Medical Center, Veterans Administration Connecticut Healthcare System and Michael E. DeBakey Veterans Administration Medical Center.

Goals/Milestones
FY12 Goals—
☑ Proposal completed and submitted to IRB

FY13 Goals—
☐ IRB approvals completed
☐ Initiate recruitment

FY14 Goals—
☐ Complete Enrollment and data collection
☐ Analyze data and submit report
Brain Training to Enhance Frontal Lobe Reasoning in Soldiers with TBI
Award #: W81XWH-11-2-0194, Training to Enhance Reasoning

PI: Daniel C. Krawczyk, Ph.D.  Org: The University of Texas at Dallas

**Study/Product Aim(s)**
- Examine the effects of Strategic Memory Advanced Reasoning Training (SMART) compared to a Brain Health Workshop (BHW) on cognition and real life outcomes in chronic traumatic brain injury (TBI).
- To examine brain changes as result of SMART versus BHW on functional Magnetic Resonance Imaging (fMRI) measures.
- To determine whether the effects of SMART versus BHW training are maintained at 3 months post-training.

**Approach**
We are evaluating a cognitive rehabilitation program, SMART, for improving attention, reasoning, and problem solving. We aim to determine whether individuals with chronic TBI benefit from SMART relative to a BHW control group. We use measures of cognition, real-life outcomes, and brain imaging (structural, functional, connectivity) to assess treatment efficacy. Comparisons are made prior to training, after training, and 3 months after the training in order to determine the effects of the training and how well improvements in cognition are maintained based on neuropsychological tests and brain imaging.

**Goals/Milestones**

**FY11 Goal** – Obtain Approvals, hire/train staff, begin enrollment and experimental procedures
- Obtain Approvals from Institutional Review Boards & HRPO
- Hire/train staff relevant to conducting testing, training, imaging
- Commence enrollment in testing, training, imaging

**FY12 Goals** – Continue with enrollment of subjects and data collection
- Enroll participants in all phases of the study
- Present preliminary results at conferences and submit manuscripts

**FY13 Goal** – Continue with enrollment of subjects and data collection
- Complete Enrollment of subjects in all phases of the study
- Present preliminary results at conferences and submit manuscripts

**FY14 Goals** – Complete study
- Complete remaining outstanding phases of the study for all subjects
- Present results and submit journal manuscripts on full project results

**Comments/Challenges/Issues/Concerns**
- None at the present time.
Brain Training to Enhance Frontal Lobe Reasoning in Soldiers with TBI
Award #: W81XWH-11-2-0195, Training to Enhance Reasoning

PI: Sandra Bond Chapman, Ph.D. Org: The University of Texas at Dallas

Study/Product Aim(s)
- Examine the effects of Strategic Memory Advanced Reasoning Training (SMART) compared to a Brain Health Workshop (BHW) on cognition and real life outcomes in chronic traumatic brain injury (TBI).
- To examine brain changes as result of SMART versus BHW on functional Magnetic Resonance Imaging (fMRI) measures.
- To determine whether the effects of SMART versus BHW training are maintained at 3 months post-training.

Approach
We are evaluating a cognitive rehabilitation program, SMART, for improving attention, reasoning, and problem solving. We aim to determine whether individuals with chronic TBI benefit from SMART relative to a BHW control group. We use measures of cognition, real-life outcomes, and brain imaging (structural, functional, connectivity) to assess treatment efficacy. Comparisons are made prior to training, after training, and 3 months after the training in order to determine the effects of the training and how well improvements in cognition are maintained based on neuropsychological tests and brain imaging.

Timeline

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<tr>
<td>Enroll subjects, conduct training, testing, and imaging</td>
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<td>Data analysis for behavioral and imaging measures</td>
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<tr>
<td>Report results in conference abstracts journal manuscripts</td>
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Goals/Milestones
FY11 Goal – Obtain Approvals, hire/train staff, begin enrollment and experimental procedures
☑ Obtain Approvals from Institutional Review Boards & HRPO
☑ Hire/train staff relevant to conducting testing, training, imaging
☑ Commence enrollment in testing, training, imaging
FY12 Goals – Continue with enrollment of subjects and data collection
☐ Enroll participants in all phases of the study
☐ Present preliminary results at conferences and submit manuscripts
FY13 Goal – Continue with enrollment of subjects and data collection
☐ Complete Enrollment of subjects in all phases of the study
☐ Present preliminary results at conferences and submit manuscripts
FY14 Goals – Complete study
☐ Complete remaining outstanding phases of the study for all subjects
☐ Present results and submit journal manuscripts on full project results

Comments/Challenges/Issues/Concerns
- None at the present time.

Updated: October 29, 2012
Study of Cognitive Rehabilitation Effectiveness (SCORE)
A randomized control treatment trial in a military population with mild TBI incurred during OEF/OIF deployment

PI: Douglas B. Cooper, PhD
Org: DVBIC

Study/Product Aim(s)
• Determine the effectiveness of cognitive rehabilitation in individuals with a history of mTBI.
• Determine which components of cognitive rehabilitation (or combination of components) are most effective.
• Determine which participant characteristics are associated with better treatment outcomes.

Approach
• The SCORE trial is a 6-week intervention with research evaluations at baseline, 3-, 6-, 12- and 18-weeks after initiation.
• Subjects are randomly assigned to one of four study arms, n=40 per group:
  1. Psychoeducational control
  2. Self-directed computerized cognitive rehabilitation
  3. Therapist-directed individualized cognitive rehabilitation
  4. Integrated interdisciplinary cognitive rehabilitation combined with cognitive-behavioral psychotherapy.

Goals/Milestones
FY11 Goal – Initiation of trial and recruitment of subjects
✔Hiring Staff-Coordinator and Research Associate March 15, 2011 and Research Psychometrist on May 2, 2011
✔Regulatory approval was received in APR 2011.
✔Completion/Regulatory Approval of Treatment Manuals on June 7, 2011
✔Recruitment started May 2011
✔First subject enrolled on July 7, 2011 with continuous enrollment to date
✔Database Implemented for Data Entry
FY12 Goals – Continued Recruitment of Subjects
☐Continue participant enrollment
☐Interim Analysis of Data
FY13 Goal – CY14 Goals - Data Analysis
☐Follow-up Data Collected
☐Final Data Analysis
☐Write papers and Dissemination

Timeline and Cost
Accomplishment: Study enrollment began JUN 2011

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<tr>
<th>Activities</th>
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<td>Recruitment/Enrollment</td>
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<tr>
<td>Follow-Up Data Collection</td>
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<tr>
<td>Data Analysis, Write Papers</td>
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**Imaging Support of Study of Cognitive Rehabilitation Effectiveness in Mild Traumatic Brain Injury (iSCORE)**

**PI:** LTC Gerald York, M.D.  
**Org:** DVBIC

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**Study/Product Aim(s)**
- Investigate longitudinal structural and functional imaging changes over time that correlate with outcome following a trial of cognitive rehabilitation
- Investigate the neural correlates of fatigue and misperception of effort as they relate to treatment outcome following mild TBI

**Approach**
Patients enrolled in SCORE!, (a cognitive rehabilitation study being conducted at BAMC) who agree to participate will be consented, enrolled and undergo MRI imaging, complete several behavioral measures a submaximal grip strength measurement and a cognitive task.

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**Timeline and Cost**

<table>
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<tr>
<th>Activities</th>
<th>FY 10</th>
<th>FY 11</th>
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<td>Obtain IRB approval</td>
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<td>Recruitment/Enrollment</td>
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**Goals/Milestones**

**FY10 Goals**
- Proposal completed and submitted to IRB

**FY11 Goals**
- Scientific review completed
- IRB approval
- Initiate recruitment

**FY12 Goal**
- Complete Enrollment and data collection

**Comments/Challenges/Issues/Concerns**
- IRB approval took longer than anticipated
- IOPI equipment was defective; had to re-order a part
- Currently enrolling patients

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Updated: 1/07/13
A Randomized Controlled Pilot Study of the Effectiveness and Feasibility of Novel Rehabilitation approaches for OIF and OEF Patients with Persistent Complaints of Cognitive Dysfunction Following TBI

**Pl:** Louis M. French, Psy.D.

**Location:** WRAMC

**Collaborating Institutions:** N/A

**Funding Source(s):** CNRM

### Aims
- Pilot study to determine the feasibility of a novel computer-based program to meet post-discharge needs for subjects complaining of deployment-related cognitive deficits.
- Feasibility will be demonstrated in terms of improvement in subjective complaints, performance on neuropsychological tests, and compliance and satisfaction with the computer program.

### Approach
- A randomized, controlled study design to evaluate the efficacy of computer-based programs.
- Patients randomly assigned to one of two computer-based cognitive training programs or to a standard of care control group receiving cognitive speech-language or occupational therapy services at WRAMC.

### Status
- Initial WR IRB Approval: March 3, 2010; CIRO/CRADA: July 13, 2010
- Continuing Review approved 24 September 2012.
- Total Enrollment: 38 of 174 (31 TBI, 7 non-TBI)
- Enrollment last quarter: 4

**Deliverables/milestones in the last quarter**
- In-service presentation to the Audiology/Speech research team on 23 August 2012.

### Key Challenges
- Many of the patients that come through the BFC are not eligible for the research protocol because they do not fit the OIF/OEF inclusion criteria or they are excluded based on the exclusion criterion that they cannot have "multiple mTBIs within 2 years of their initial BFC appointment."
- For eligible, consenting patients, holidays and leave interfere with daily computer session attendance, or the patient may be discharged from Walter Reed prior to completing the full 6 weeks of computer sessions.
- Potential participants are eager to try the computer programs and don’t wish to be assigned to the standard of care control group.

**Deliverables/milestones anticipated in the next year**
- Recruitment at Ft. Belvoir expected to help study reach sample size (174).
- Begin running analyses on the pre and post data for prospective study.
Using a Simulator to Enhance Cognitive Recovery After Mild Traumatic Brain Injury

**PI:** Melissa Amick, PhD  
**Location:** VA Boston Healthcare System  
**Collaborating Institutions:** N/A  
**Funding Source(s):** VA RR&D

### Aims

- To determine whether participants with a history of mild TBI and/or PTSD and self-reported driving difficulties perform more poorly than healthy controls on an assessment of driving abilities and to examine the association between cognitive and behavioral symptoms with driving abilities.

### Approach

- 100 OEF/OIF veterans with a history of PTSD and/or mTBI and 50 age- and education matched control participants will complete: a simulated driving assessment, neuropsychological tasks, and questionnaires measuring psychological symptoms, driving history, and fatigue.
- Primary outcome measure is number of errors committed on the simulated driving assessment. Secondary outcome measures will include cognitive and behavioral variables.

### Status

- Initial IRB Approval: VAHS local IRB approval 10/19/09  
- Enrollment: 65 of 150

### Key Challenges

- **Challenge:** continued funding  
- **Solution:** resubmission of grant  
- **Challenge:** limited staff  
- **Solution:** looking for funding to continue project

### Deliverables/milestones in the last quarter

- Local IRB approval
- Approved amendment to broaden recruitment through collaboration with other local on-going studies of mTBI/PTSD
- Enrollment of first 50 participants with enrollment continuing
- Identification of driving simulator outcome measures
- Renewal submitted 6/2010 (scored, 31st %ile)
- Resubmission to RR&D, 12/2011
- Data presented at INS meeting 2/2011

### Deliverables/milestones anticipated in the next year

- Preliminary findings on the clinical utility of driving assessment submitted for presentation and scientific meetings and publication.
A Randomized, Controlled Trial of Interactive Metronome Technology for Remediation of Cognitive Difficulties Following Blast-Related TBI

PI: CDR Renee Pazdan, MD  Org: DVBIC – Fort Carson

Study Aim(s)
- Determine whether the addition of Interactive Metronome (IM) training to treatment as usual (TAU) in patients with moderate to mild TBI due to blast results in greater improvements in attention and memory; better secondary outcomes such as postconcussion symptom status, vocational functioning, and quality of life; and improved normalization of electrocortical functioning, immediately and at 6 months.

Approach
- A randomized, controlled trial of 15 sessions of IM over 5 wks compared with 5 wks of TAU in those with mild to mod TBI due to blast.
- Patients randomized to IM training will complete 15 sessions over 5 wks
- Primary outcomes will include attention and memory functioning, measured prior to the start of treatment period, one week following the end of treatment period, and 6 months after treatment period.
- TAU patients will be offered IM after completing 6 month assessments.

Goals/Milestones

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<td>Regulatory Approval and Initiation of Recruitment</td>
<td>Participant Recruitment and Interim Analysis</td>
<td>Complete enrollment, delivery of treatment</td>
<td>Complete analyses and dissemination of findings</td>
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<td>Recruitment of wave one; initiation of post treatment assessments</td>
<td>Complete post-treatment and follow-up assessments</td>
<td>Begin analysis of follow-up data and dissemination of findings</td>
<td>Complete follow-up assessments</td>
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<td>Initiate interim analyses and report of initial (7 week) findings</td>
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Interim analyses indicate that IM treatment is associated with greater improvements in performance on neuropsychological tests compared to treatment as usual; evidence of brain plasticity and effect of building timing awareness and response-ability.

Timeline

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<td>Complete 7 week and 6 month Assessments for IM and TAU pts</td>
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<td>Post Follow up IM treatment delivery to TAU group members</td>
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<td>Data Analysis and Dissemination of Findings</td>
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Updated: 22OCT2012

Comments/Challenges/Issues/Concerns

- Research staff no longer blinded to randomization; putting additional staff in place to recruit last 5 subjects
- Neuropsychological tests of memory and attention showed significant increases at 7 week testing in the IM group relative to those in the control group.
Traumatic Brain Injury Rehabilitation: A controlled, randomized multicenter study of interdisciplinary programs with adjuvant pharmacotherapy

PI: Larisa Kusar, M.D., Barbara Sigford, MD, PhD
Location: Minneapolis VA Health Care System
Collaborating Institutions: WRAMC, Richmond, Palo Alto and Tampa VA PRCs

Funding Source(s): DVHIP/DVBIC

Aims

• To integrate clinical research with care so as to enhance care both at present and in the future.” Specific objectives for Phase I include: (1) establishment of a national DoD/DVA TBI registry; (2) appropriate follow-up of DoD/DVA TBI patients; (3) standardized sequential evaluations of long-term outcome of TBI patients; (4) enhancement of care by integration with clinical research; (5) establishment of multicenter DoD/DVA network of hospitals for collaborative research. Phase II: (6) the prospective evaluation of TBI rehabilitation programs.

Approach

• Phase I, data will be collected and scored by professionals in the area being evaluated. Data will be collected at baseline, 6, 12 and 24 months. Evaluation is expected to take approximately 3 days.
• Phase II, patients will be assigned to one of two treatment protocols in a prospective, randomized fashion. Enrollments were completed in 6/2003. Enrolled patients were evaluated at baseline, 6, 12 and 24 months using the same data collection formats as Phase I with the addition of a measure of social pragmatics in the evaluation.

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<td>Data Analysis</td>
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<td>Dissemination</td>
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Status

• Initial IRB Approval: April 23, 1993
• Enrollment: 142 of 190 (at this site) of which 98 were surrogate consents; 4 withdrew by self. Enrollment last quarter: 0
  • Two phase study Phase I: 76 enrollees, Phase II: 66 enrollees
• Study is closed to enrollment, Last subject enrolled/consented 2004
• Continuing Review submitted 6.6.2012; All approvals rec’d 10.2.2012
• Documentation of approval sent to Loretta Polite 10.3.2012

Key Challenges

• Ongoing applications for IRB annual review.
• Consulting with IRB for appropriate storage of materials for open study.
• Storage of Study Documentation
• DVBIC HQ scanning all documentation for management of archived records
• Per ORO, no original VA documents may be destroyed.

Deliverables/milestones to date

• Amendment to Phase I: 4.10.2007
• Amendment to Phase II: 6.29.2007
• Amendment to Phase II: 5.23.08
• Amendment 3.10.2009 re: location of data review to take place at WRAMC Q4 FY12

Deliverables/milestones anticipated in the next year

• Minneapolis data in process of review and entering into electronic database.

Results comparing cognitive didactic and functional-experiential approaches to brain injury rehabilitation indicated improved but similar long-term global functional outcome. Participants in the cognitive treatment arm achieved better short-term functional cognitive performance than patients in the functional treatment arm.
Study/Product Aim(s)

• To assess the effectiveness of computerized instructional tools as an adjunct to standard community integrated brain injury rehabilitation.
• To examine service members’ experiences and satisfaction utilizing computerized intervention tools.
• To inform participant instructional tool selection to maximize potential benefit.

Approach

• Service members with TBI will be recruited through DVBIC Charlottesville.
• Participants will be randomly assigned to either an unstructured interactive computer activity with clinician interface or to the identified instructional modules with clinician interface, as an adjunct to the existing rehab program.
• Pre and post assessments and program outcomes (including functional and vocational) will be assessed and analyzed for both groups.
• Participants will be interviewed regarding feedback, perceived benefit and satisfaction with the intervention.

Goals/Milestones

FY11 Goals
✓ Recommended content modifications sent to software programmers.
✓ Grant applications submitted by ISI in order to fund software enhancements per recommendations
☐ Finalize software upgrades/enhancements

FY12 Goals
☐ Secure funding to finalize software upgrades/enhancements
☐ Train staff on software utilization
☐ Initiate subject recruitment and implementation of intervention

FY13 Goals
☐ Analyze data and disseminate results

Comments/Challenges/Issues/Concerns

• Securing adequate sample size.
• Software development/upgrading taking longer than anticipated
Hope, Healing, Discovery and Learning for Traumatic Brain Injury and Psychological Health
Assessing the impact of mTBI on multisensory integration while maneuvering on foot

Designate: TBI + Hearing + Vestibular

PI: Brungart, Douglas  Org: Walter Reed NMMC/ National Intrepid CoE

Problem, Hypothesis and Military Relevance

**Problem:** TBI is known to produce substantial deficits in auditory, visual, and vestibular processing, however the impacts it has on multisensory integration are not well known.

**Military Relevance:** This effort will directly attack one of the most critical issues regarding the re-deployment of soldiers with TBI: the ability to move, shoot, and communicate on the battlefield.

**Technical Approach:** This study will take an aurally-aided visual search paradigm that has been shown to be effective for assessing audio-visual integration in stationary environments and a well established auditory and auditory-visual speech recognition task and put them to a moving platform that will greatly increase the sensory load and simulate dismounted combat operations.

Proposed Solution

**Objective:** Evaluate auditory-vestibular-visual interaction in normal and TBI participants with an aurally-aided visual search task and a speech recognition task with relevance to dismounted military operations.

**Description of Effort:** We will modify the CAREN simulator at the National Intrepid Center of Excellence to include a spatialized speaker array. This will allow us to conduct true multisensory integration tasks.

**Benefits of Proposed Technology:** By incorporating multimodal tasks that test the most difficult multisensory environments involved in dismounted patrolling, we expect to: 1) Enhance our ability to diagnose multisensory problems in TBI patients; 2) Inform fitness-for-duty standards; and 3) Examine potential methods for rehabilitating TBI-related sensory deficits.

<table>
<thead>
<tr>
<th>Activities</th>
<th>FY 13</th>
<th>FY 14</th>
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<tbody>
<tr>
<td>Phase 1: Implement spatial sound array in CAREN</td>
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<td>Phase 2: Establish baseline search times for visual, auditory and aurally aided tasks for normal and TBI participants</td>
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<td>Phase 3: Develop a model of visual search time for normal participants with degraded vision and audition. Evaluate auditory-visual speech perception in dynamic multisource environments.</td>
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Project Title: Pilot Study to Assess the Application of Haptic Technology to Functional Improvement in Persons with Mild and Moderate Traumatic Brain Injury
Principal Investigator: Leighton Chan, M.D., M.P.H.

ABSTRACT

Traumatic Brain Injury is a complex condition that is not completely understood. Our laboratory is working towards determining the feasibility of haptic technologies to assess and treat a population of individuals who have mild to moderate TBI. We are using the haptic along with a computer system to create challenging and engaging virtual environments and extract objective measures concerning their orientation, motor, and cognitive skills. We have performed a pilot study using college students and showed that they were highly engaged, and that objective measures could be extracted. These measures showed that fine motor learning occurred over a course of three trials in the virtual environment. We have since expanded our virtual environments to include a gun disassembly task, sandwich making task, and a letter spelling task which has similarities to Scrabble. We have also programmed two spatial orientation tasks, a maze that can be navigated from two viewpoints, within or above, and a network of corridors that is navigated only from within.

We have received feedback from Brain Injury Services, Inc., an organization that provides services to persons with TBI. The group came to the lab to provide insight on how to improve our physical and virtual environments. We have a protocol in place for which we will be collecting data from these TBI patients and others recruited through the CNRM Recruitment Core. We will be looking at the ability of the virtual environments to engage and challenge the individuals as well as determining objective measures for analysis. We will also be comparing outcomes from the virtual environment to those from classic measures, including the Purdue Pegboard and Wolf Motor Function Test.
Project Title: Effects of Rapid Reciprocal Exercise vs. Light Therapy in TBI  
Principal Investigator: Diane L. Damiano, Ph.D.

ABSTRACT
Objectives:
We will: 1) compare performance of healthy volunteers and ambulatory adults with traumatic brain injury (TBI) on a range of motor, neurobehavioral and brain imaging outcomes; and 2) evaluate effects of rapid, reciprocal arm and leg exercise with an elliptical trainer on high-level motor coordination and balance, and neurobehavioral and cognitive functioning in persons with TBI. Outcomes will be compared to those from a novel intervention for improving mood and cognition, Bright Light Therapy (BLT). Brain connectivity and changes in connectivity in response to interventions will be quantified. We hypothesize even highly functional adults with TBI will have poorer scores on all measures than controls; exercise will lead to significant improvements in motor performance and balance compared to BLT; and neurobehavioral and cognitive function will improve with both interventions. We further hypothesize that improvements in cortical connectivity and representation will relate directly to functional ones.
Study Population:
80 adults (50 with TBI) will be recruited so that 20 with TBI and 20 healthy volunteers complete the study. Only the TBI group will receive intervention.
Design:
Healthy controls with have a single assessment that includes motor, neuropsychological and brain imaging tests. Participants with TBI will perform both interventions: 3 months of fast elliptical training or Bright Light Therapy in randomized order with a four-week washout period between them. Assessments will occur at 0, 3, 4, and 7 months. The exercise device will be an elliptical trainer that exercises the legs and arms with the emphasis on maintaining a fast speed. Mild resistance will be provided initially and progressively increased once speed is optimized. An in-home light box will be used for the other intervention. Each intervention will be performed in the home 5 days per week for 30 minutes, over 12 weeks.
Outcome Measures:
Performance on complex motor & balance tasks will be assessed with 3D motion capture & EMG, the Smart Balance Measurement System and the High Level Mobility Assessment Tool (Hi-MAT). Primary outcomes are Hi-MAT score reaction time during balance testing and the Hamilton Rating Scale for Depression (Ham-D). Secondary outcomes will include walking speed and device cadence, PTSD Checklist (PCL-17), and relevant portions of the Automated Neuropsychological Assessment Metrics (ANAM) battery, among others. Cortical connectivity will be quantified using resting state functional connectivity magnetic resonance imaging (MRI) and Diffusion Tensor Imaging (DTI), which evaluates white matter tracts. Cortical activation patterns will be quantified with fMRI.
Conclusions

- In the military healthcare system, we focus on TBI rehabilitation in a relatively short-term window (approx 1 year) as by that time it is typically clear whether or not the Service Member should be retained on active duty
  - More severely injured SM’s move to the VA Polytrauma Network
- We support cognitive rehabilitation research efforts within both DoD and VA as well as in academia and industry
  - Issues such as clinical definitions, evolving understanding of the natural history and pathobiology of TBI, and evolving understanding of the need for accurate and specific outcome measures currently drive our research process.
  - We will be developing a more detailed strategic plan for cognitive rehab in CY 13 based upon lessons learned in this and other TBI research arenas.
- Cognitive rehabilitation in “mild” TBI will remain a challenge to assess because of the heterogeneity of the injury and its co-morbidities as well as the huge number of confounding variables introduced in the outpatient setting. Large, well designed and controlled studies will be necessary.
- Our understanding of neuroplasticity continues to improve and gives us a sense of optimism as we move forward.
  - Improving capabilities of functional imaging and neurophysiological assessment technologies will help us develop a better understanding of how these interventions work and how they can be improved.
Research is to see what everybody else has seen, and to think what nobody else has thought.

- Albert Szent-Gyorgyi