Brain Health and Fitness Overview

CAPT C. Douglas Forcino
Director, Military Operational Medicine Research Program
Chair, Joint Program Committee 5 for Military Operational Medicine
US Army Medical Research and Materiel Command
24 March 2015
The views expressed in this presentation are those of the author(s) and may not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government.
Brain Health: The state of cognitive, psychological, and behavioral fitness which enables peak human performance through the brain’s capabilities of attention, reasoning, decision making, problem solving, learning, communicating, and adapting.
PANEL MEMBERS

• COL Dallas Hack-Traumatic Brain Injury

• LTC Chessley Atchison-Environmental Sensors for Possible Concussive Events

• Dr. Thomas Balkin-Fatigue Management for the Soldier

• Dr. Raymond Genovese-Challenges for Developing New Pharmacologics for the Treatment of PTSD

• Mr. Michael Husband-Neurotrauma and Psychological Health Advanced Development
Traumatic Brain Injury
Overview

COL Dallas Hack
Office of the Principal Assistant for Research & Technology
US Army Medical Research and Materiel Command
24 March 2015
Environmental Sensors for Possible Concussive Events

LTC Chessley R. Atchison
Office of the Principal Assistant for Research & Technology
US Army Medical Research and Materiel Command
24 March 2015
To increase understanding of environmental sensors for the detection of possible concussive events.

• Points

- Sensor Requirements (G’s Measured, PSI measured, battery life, etc.)
- Sensor Wear (Fit & Function)
- Sensor Validation
- Algorithm Development (Math necessary to capture the data)
- Algorithm Validation
- Ultimate Goal: Dose Response Curve that predicts the probability of injury based on sensor data!
Training Examples

Airborne Training

Combatives Training
Artillery Training
Fatigue Management for the Soldier

Thomas J. Balkin, Ph.D.
Behavioral Biology Branch, CMPNS, WRAIR
US Army Medical Research and Materiel Command
24 March 2015
To describe the unique need and capability for implementation of a comprehensive fatigue management system (FMS) in military operations.

• Points
  - *Sleep loss impacts both short-term performance/military effectiveness*
  - *Sleep loss is ubiquitous in military operations*
  - *Three-component military FMS will be complete within 3 years*
  - *Remaining need: the platform (e.g., smartphone app?) for fielding of the FMS*
Sleep Loss is characterized by brain deactivation – especially in brain regions that mediate cognitive performance and alertness.

- Performance deficits often result from the combined effects of sleep loss and circadian rhythm misalignment (e.g., nighttime operations).

72 Hours of Total Sleep Deprivation: Effect on Arithmetic Task Performance

Throughput (Percent of Baseline)

Sleep Deprivation (Hours)
Sleep & Self-Reported Mistakes in OIF

Reported having an accident or mistake that affected the mission

Source: MHAT V data

Average hours of sleep per day

- 4 or less
- 5
- 6
- 7
- 8

Reported having an accident or mistake that affected the mission

- 14%
- 12%
- 10%
- 8%
- 6%
- 4%
- 2%
- 0%
Sleep Watch Actigraph

- Because that which cannot be measured in the field cannot be managed in the field

An Armamentarium of Fatigue Countermeasures

- Stimulants to restore/maintain performance during sustained/continuous operations when there is little or no opportunity to sleep
- Sleep inducers/counteractants to enhance recuperative sleep when needed

Alertness Management for Military Operations (AMMO)

- So that operational performance degradation can be anticipated and planned for, and informed decisions regarding dosage and timing of countermeasures can be made.
The Final Product

Alertness Management for Military Operations

Soldiers wear wrist actigraph for weeks/months. Activity data serves as input ...

...to sleep scoring algorithm, which in turn serves as input to AMMO....

...the results of which are displayed on the Soldiers’ personal technology, where different scenarios can be explored (e.g., what if I take a 30-minute nap at 1400 hrs? What will my performance capacity be at 0200 Hrs tomorrow if I don’t get any sleep between now and then? How much benefit will I get from drinking a cup of coffee now, and for how long? etc.)
Challenges for Developing New Pharmacologics for the Treatment of PTSD

Raymond F. Genovese, PhD
Behavioral Biology Branch, CMPN, WRAIR
US Army Medical Research and Materiel Command
24 March 2015
Objectives

- Therapeutic protocols for PTSD guided by precision medicine.
- Advanced clinical development of PTSD medication in a military population.

ClinicalTrials.gov

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.
Unique Challenge of PTSD Drug Development

Preclinical Models
- Well-established nociception models (e.g., Tail-Flick Hot-Plate) that demonstrate predictive validity.

Gold Standard Compounds
- e.g., Morphine
- e.g., Chloroquine & Artesunate

Extrapolation
- Facilitated by preclinical models with predictive validity.

Analgesia

Malaria
- In vitro and in vivo Parasite clearance models that demonstrate predictive validity.

PTSD
- Many, but none that have, thus far, demonstrated predictive validity.

Challenged by the difficulty of demonstrating preclinical efficacy.
New molecules or new applications of molecules demonstrating a convergence of positive data on multiple existing preclinical tests.

Clinical trials targeting innovative and evidence-based approaches, novel pathways, novel applications and combination (pharmacologic and psychotherapeutic) strategies.

New preclinical tests showing “drive-by” efficacy in a few select instances.
Opportunities and Partnerships

Novel compound / application → GLP STUDIES → IND → Phase I & 2 Clinical Trials
Objective

- Ability to identify Service Members who may be at higher risk for attempting suicide & interventions to prevent suicide attempts.
Suicide Prevention Initiatives

Funded through the Defense Health Program and managed by the Military Operational Medicine Research Program (MOMRP), this innovative cutting-edge research aims to enhance the military’s ability to quickly identify those at risk for suicide and provide effective evidence-based prevention and treatment strategies.

https://www.msrc.fsu.edu/
• Validated and effective training for bystander intervention.
• Validated and effective training for leader intervention.
• Self-management strategies for reducing suicidal thoughts.
Neurotrauma and Psychological Health
Advanced Development

Michael Husband
PM NPH
US Army Medical Research and Materiel Command
24 March 2015
Neurotrauma and Psychological Health Project Management Office

**Mission:** To coordinate and oversee advanced development and acquisition of medical products in Traumatic Brain Injury (TBI) and Psychological Health (PH) that will meet validated Warfighter needs through the execution of approved research, development, and acquisition (RDA) programs.

**Vision:** Leading the development of innovative, evidence-based solutions for TBI and PH.
DoD Advanced Development

S & T

Proof of Concept

• Partnerships
• Intellectual Property
• Acquisition Strategy
• FDA Regulatory Management
• Clinical Development
• Verification and Validation
• Testing
• Manufacturing

Valley of Death

Medically Ready Force
Psychological Health

1. Drug
   - Repurposing
   - Novel molecular entities
   - State of the Science Summit – November 2015

2. Biomarker
   - Use in diagnostics
   - Use to assess endpoints in clinical trials
   - Use to identify targets for intervention

3. Device
   - Treatment of Posttraumatic Stress Disorder (PTSD): Invasive and Non-invasive
   - Suicide prevention: Detection of dynamic risk

4. Knowledge Product
   - Enhancing psychotherapies with medications or devices
   - Clinical implementation
1. Drug
   - Treatment of injury
   - Treatment of symptoms

2. Biomarker
   - Baseline risk
   - Acute diagnosis
   - Identification of potential subtypes
   - Prognosis
   - Use to assess endpoints in clinical trials
   - Use to identify efficacy of treatment

3. Device
   - Treatment of TBI: Invasive and Non-invasive
   - Diagnostic: Aid to clinical assessment and patient management

4. Knowledge Product
   - Standards for clinical assessment and treatment
   - Clinical implementation
Product Life Cycle

6.1 TRL 1-3
Discovery

6.2 TRL 4-5
Preclinical

6.3 TRL 5-6
Phase I-II

6.4 TRL 6-7
Phase II-III

6.5 TRL 7-8
Phase III

Premarket approval process (PMA) or 510(k)

Procurement
TRL 8-9

Production & Deployment
Phase
FDA Approved
It is estimated that over 2.3 Million US Service Members deployed 2001-2014

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<thead>
<tr>
<th>Incidence of TBI</th>
<th>Incidence of PH Conditions</th>
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<tr>
<td>313,816 documented TBIs (2000-3QFY14) with over 80% classified as mild TBI and 9% moderate/severe TBI, 9% Unknown¹ (over 80% of TBIs are diagnosed in a non-deployed setting. TBI will remain a military concern long after withdrawal from Afghanistan.)</td>
<td>Mental Disorder</td>
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<td>• The average costs for the first year of treatment for returning veterans $11,700²</td>
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<td>• Direct medical costs and indirect costs of TBI, such as lost productivity, totaled an estimated $60 billion in the United States in 2000.⁹</td>
<td>PTSD and Major Depression</td>
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<td>Average civilian hospital stay: Mild - 1 day per event; Moderate – 6 to 7 days per event; Severe - 17-18 days per event. Rehabilitation length of stay average 55 days.</td>
<td>• 2001 – 2008: $4 - $6.2 billion = total cost for PTSD and depression in the first two years following redeployment³</td>
</tr>
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<td>According to the CDC, falls are the leading cause of TBI, while motor-vehicle-traffic injury is the leading cause of TBI death. Death rate from CDC = 3% of all TBIs.⁴ TBI is a contributing factor to a third of all injury-related deaths in the US.⁸</td>
<td>• 11-20% of OEF/OIF Veterans have PTSD¹⁰</td>
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<td>• Average costs for the first year of PTSD treatment for a returning veteran = $8,300²</td>
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<td>Suicide</td>
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<td>• Beginning in 2010: second-leading cause of death for active duty service members, behind war injuries.⁶</td>
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<td>• 200 deaths by suicide in active duty service members in 1998, rising to 349 in 2012⁷</td>
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Questions?

For additional questions after the conclusion of the conference, send an email message to usarmy.detrick.medcom-usamrmc.mbx.mmpd@mail.mil