

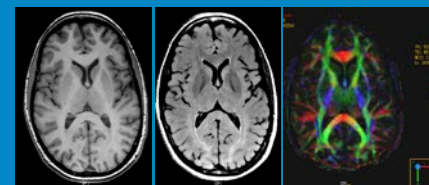


Role of VHA Office of Research and Development in De-Risking Multimodal Therapy Development

The VHA Office of Research and Development

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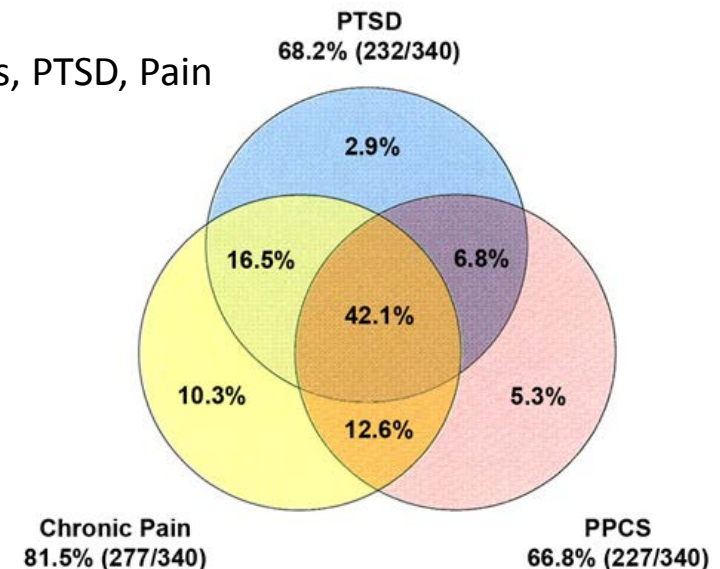
Background

- First experience in multimodal therapies
 - 1980s Fetal brain transplants
 - Sensorimotor lesions in rats
 - Balance Beam task
 - Transplants did better than no transplant and almost as well as sham-controls
 - High speed cinematography revealed that recovery did not involve regaining the same motor program, but results were equal
 - In reality most preclinical studies are multimodal
- Second experience
 - Faculty in Emergency medicine, Emory University, Grady Memorial in Atlanta.
 - Vast majority of brain injuries are polytrauma
 - Not only multimodal therapies, but multimodal injury
- Third experience
 - VA Research Administration
 - TBI as a chronic condition with co-morbidities

Structure:
Injury modeling → Diagnostic Development → Therapy development →
Clinical Trials → Implementation

Nature of TBI From OIF/OEF/OND

- Concussion/mTBI
 - Overwhelmingly mild TBI
 - Three P's: Persistent Post-Concussional Symptoms, PTSD, Pain
- Moderate to Severe
- Co-Occurring Conditions
- Long-term Effects of Injury
- Co-Occurring Conditions
 - Sensory (Peripheral or Central)
 - Psychiatric
 - Mobility (Amputation, SCI, or Brain)
- Cognitive
- Executive Dysfunction
- Endocrine



Multimodal treatments in rehabilitation (TBI)

- **Headache Care:** Normalize sleep cycle with trazadone 100 mg at night, utilize temporalis muscle biofeedback with psychologist, mobilize cervical paraspinals and work on sitting neck posture in PT sessions, and modify job site and work ergonomics with OT sessions
- **Dizziness:** Use Liberatory Technique in PT, offer trial of Meclizine patch, work on eye tracking in OT, practice relaxation strategies in psychology
- **Memory Deficits:** Cognitive Rehabilitation strategies with Speech Pathology, Normalize Sleep/Wake Cycling through meditation and enhanced sleep hygiene with Psychology, remove sedating antihypertensives and teach an aerobic exercise program in Kinesiotherapy
- **Irritability:** Teach strategies for manager management in psychology, Vocational Rehabilitation to work on job skills with co-workers, trial of tegretol for behavioral dyscontrol, PT sessions for thermal therapy and range of motion for posterior headaches worsening behavior
- **Photophobia:** OT sessions for how and when to use adaptive aides (dark glasses), optometrist to work on visual reintegration therapy, Psychologist to assist with Exposure

Potential Risks of Multimodal Therapy Research in VA

- Patient safety-
 - This not only potential safety issues with treatments also data security.
 - Data security becomes an issue when collaborating with non-VA partners
- TBI population itself, especially those with moderate to severe brain injury
 - Vulnerable population, Fatigue, agitation
 - In the mTBI population- lack of self-realization of deficits, comorbid e.g., psychological health
- TBI Subpopulations
 - How to identify? Need biomarkers, no clinically validated biomarkers exist.
- Not being aware of knowledge gained by other Federal Funding Agencies
- “Valley of Death”- Currently no direct SBIR-like mechanism to help bridge the gap.

How Does VA/ORD De-Risk Multimodal Therapy Research?

- Intramural Research Program
 - Control of programmatic decisions, peer-review, and regulatory oversight
 - Integrative Healthcare system
 - Researchers have a stake in therapy development
 - Researchers are embedded in the system
 - Precision Medicine – Million Veterans Program
 - Programmatic Guidance
 - Tracking the project and recruitment
 - Supplying resources and/or infrastructure when necessary
 - Translate to the next phase or translate back improve approach
- Preclinical → Clinical Trial → Cooperative Studies → Implementation



How to does VA Research De-Risking Benefits future Development of Multimodal Therapies

For Brain Injury research, having an Executive Order to motivate policy is helpful.

- National Research Action Plan to Improve Mental Health for Servicemembers, Veterans and their Families
 - Created a formal partnership between the Federal agencies that fund TBI research
 - Visibility of ongoing projects to prevent duplication and to explore synergism
 - Call outs in the plan for:
 - a Research Consortium to study chronic effects of TBI
 - Tissue repositories
 - Biomarker development
 - Data sharing
 - In addition to the Chronic Effects of the Neurotrauma Consortium, the structure created by the Plan has lead to the linkage of the Consortium to other initiatives, e.g., TBI Endpoint Development (TED) Initiative.

Internally, the VA has re-interpreted the guidance on Public-Private Partnership policy.

- Will allow for potential Industry partnerships through the VA Center for Innovation