Examining TBI as a Chronic Condition Session 2 Participants Moderator & Speaker

Primary Speaker



Professor and Vice-Chair Faculty Development **UPMC Endowed Translational Research Chair** Dept. Physical Medicine & Rehabilitation

Professor, Neuroscience Professor, Clinical & Translational Science Institute Associate Director Rehabilitation Research Safar Center for Resuscitation Research University of Pittsburgh, Pittsburgh PA, USA



Associate Professor of Neuroscience, School of Biochemistry & Immunology, Trinity College Dublin, Ireland,

Adjunct Associate Professor, Shock, Trauma, & Anesthesiology Research Center University of Maryland School of Medicine (UMSOM), Baltimore, MD, USA.

Examining TBI as a Chronic Condition

Session 2: Neuropathophysiological Mechanisms Underlying TBI as a Chronic Condition

Session Objectives:

- Examine the state of the evidence on the biological basis for TBI as a chronic condition.
- Identify research gaps or barriers to advancing understanding of the • lasting health effects of TBI.





Institute

ΝΛΤΙΟΝΛΙ UPMC Rehabilitation ACADEMIES

Sciences Engineering Medicine



Trinity College Dublin Coláiste na Tríonóide, Baile Átha Cliath The University of Dublin

Session Overview

- Overview central features of chronic TBI pathology observed with moderate to severe TBI and/or repetitive TBI
- Address key functions of, and communication between, the systemic immune system & the CNS
- Describe the host response to TBI as a whole-body injury
 - impacts on CNS dysfunction and repair
 - multi-organ system *dysfunction/resilience* to subsequent illness and chronic conditions.
- Discuss the potential long-term biological impacts of the host response to TBI
 - accelerated biological aging and effects on longevity,
 - Pathological basis of cumulative comorbidity burden as one "ages with their injury"
- Delineate the capacity for biomarkers-based research
 - To reflect TBI pathology over time
 - To capture how inflammatory and other injury mediators can be linked to function
 - To inform risk for secondary chronic conditions,
 - To prognosticate recovery
 - To identify relevant treatment targets.

Considering Chronic TBI Associated Pathology in the Context of Health, Chronic Conditions & Function

Health Defined

- Health is historically defined in the medical model as the absence of any chronic disease (i.e. chronic health conditions)
 - The definitions associated with chronic disease/health condition definitions vary, but often symptoms and pathology persist >3-12 months
- Function is a leading indicator of health, and assumptions about health are <u>based on</u> <u>level of function</u>
- Health in the context of chronic TBI its associated chronic conditions and pathology
 - Is a **state of balance** where *individuals function* in their social and physical environments with variable degrees of success.
- **Translational Research Thesis**: Understand the underlying biological effectors of chronic TBI pathology, and its impact across body systems and multiple domains of function, using a biomarkers-based approach
 - may inform individual recovery trajectories, prognostication, and treatment approaches that improve function.

TBI translational rehabilitation research in the 21st Century: exploring a Rehabilomics research model



EUR J PHYS REHABIL MED 2010;46:549-55

Rehabilomics: Mapping Biomarkers to the WHO-ICF



ICF: Bridging the Taxonomy Gap Between Disease, Disability, Health & Function...

Rehabilomics Exemplar Assessing Inflammation and Cognition – using ILS

- Cognitive impairment post-TBI is a central component to survivor outcomes such as the ability to return to work, live independently, and participate in leisure activities.
- Used weighted inflammatory load score, as measure of inflammatory burden on cognition in a cohort with msTBI.
- <u>Overall cognitive composite scores</u> were created as an average of normalized mean T-scores from neurospsychological test measures representing the following cognitive domains: <u>verbal fluency</u>, <u>memory</u>, <u>attention/ processing speed</u>, and <u>executive function</u>

Covariate Adjusted Linear Regression–wILS vs. 6 M Overall Composite

Variable	β	p-value	Adjusted R ²
Age	0.02489	0.6138	0.2436 for base model
Gender	-2.40644	0.2287	0.3264 adding ILS
Years Education	1.70690	<.0001	
Best in 24 GCS	0.88527	0.0013	=0.0828 difference
Overall Weighted ILS	-22.52384	0.0003	33.99% improvement

NANILJ

ILS Associations Pushing through the ICF: Functional Cognition and QOL

β=0.510, p<0.001

Overall cognitive



- Comprehension
- **Expression**
- Social Interaction
- **Problem Solving**



FIM cognition

Inflammation influences other functional endpoints through its impact on cognitive performance deficits

6-Month Inflammatory, Autoimmune, Vascular,& CNS Damage Marker Matrix:



Long Term Vision for Biologically Grounded, Personalized, Community-Based Care for Chronic TBI



Overall, our long-term vision is for a scalable, integrated Point-of-Care Biomarker and telehealth technology suite for chronic, community-based care for individuals living with chronic TBI that provides <u>Personal Biology</u> readouts for risk stratification and clinical decision making over time to personalize approaches to chronic care in populations dealing with the long-term and late effects of TBI.

Session 2: Discussion Period





UPMC Rehabilitation NATIONALACADEMIES Medicine Institute

Sciences Engineering



Trinity College Dublin Coláiste na Tríonóide, Baile Átha Cliath The University of Dublin

Temporal Perspectives on TBI As a Chronic Condition

Prognostic and Treatment Opportunities Across the Continuum of Care

TBI translational rehabilitation research in the 21st Century: exploring a Rehabilomics research model



EUR J PHYS REHABIL MED 2010;46:549-55

Rehabilomics research and implementation programs span the continuum of care by utilizing biomarkers to characterize bio-psychosocial links between TBI pathology, chronic conditions, and functional recovery.

A. K. WAGNER

GOAL: operationalizing TBI biomarkers to capture the interplay over the care continuum between TBI damage processes, injury and recovery course, and TBI repair that affect function.