

Chronic Effects of Neurotrauma Consortium



DAVID X. CIFU, MD (VCU)

RAMON DIAZ-ARRASTIA, MD, PHD (USUHS)

RICK WILLIAMS, PHD (RTI)

FUNDING AGENCY: DOD / VA

FUNDING DATES: 2013 - 2018

TBI in the Modern Battlefield



Is it really new?

World War I (The Great War) 1914-1918)



Large numbers of combatants developed a spectrum of psychiatric/behavioral symptoms which precluded their being able to continue to serve on the battlefield. Most of these patients were categorized as either having NYDN (Not Yet Diagnosed, Neurologic) or simply “shell shock”.

Report of the War Office Committee of Enquiry into “Shell Shock” (Southborough Committee) 1922

- Testimony from many experts expressed belief that “shell shock” was a form of **malingering**, at best, or even **cowardice**.
- There was a general feeling that patients with shell shock were **lacking in moral fiber**.
- “No case of psycho-neurosis or of mental breakdown, even when attributed to a shell explosion or the effects thereof, should be classified as a battle casualty.”
- Shell shock was not a valid diagnostic entity and the use of the term should therefore be **banned**.

The View from 1966



Robert B. Daroff, MD

Consultant Neurologist, 93rd Evacuation Hospital, Long Binh, Republic of Vietnam

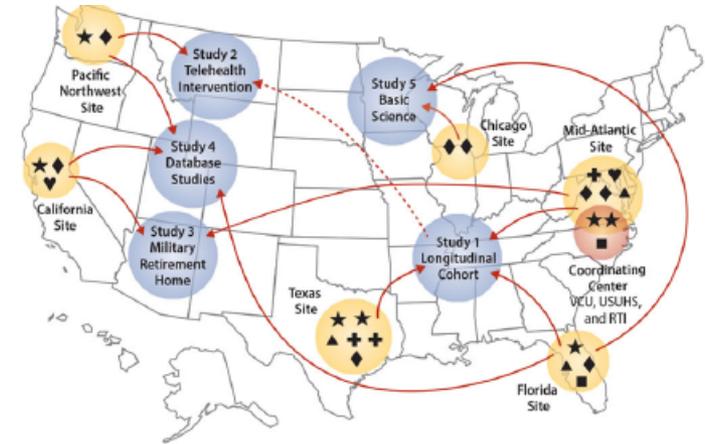
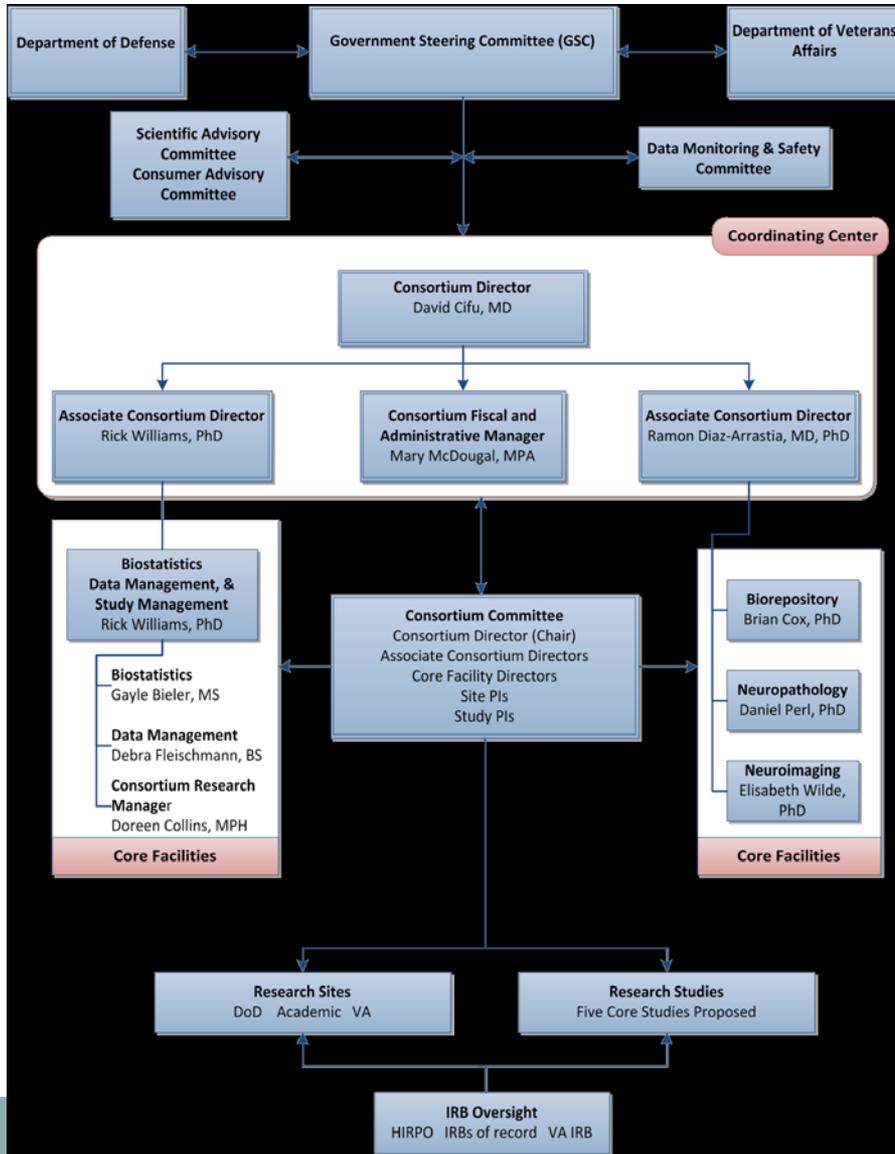
“Post-concussion syndrome was common and I treated them symptomatically with a restricted duty profile for a few weeks. If the symptoms persisted, I always stated that the problem ‘was no longer organic’ and made a psychiatric referral. I was convinced that incapacitating headaches and dizziness after one month of minor head trauma was non-organic. My psychiatric colleagues diagnosed ‘character disorder’ on almost all psychiatric patients who were not psychotic or clinically depressed.”

TBI in the Modern Battlefield

- A substantial number of troops deployed in Iraq and Afghanistan have experienced TBI¹
 - 4.9% with loss of consciousness
 - 10.3% with altered mental status
 - 73 – 79% related to exposure to blast or explosion
- Multiple TBI episodes are common
- Exposure to TBI (particularly with LOC) associated with:
 - Headache
 - Fatigue
 - Sleep Disturbance
 - Memory Problems
 - Balance Problems
 - Concentration Problems
 - Irritability

¹ Hoge et al, *NEJM* 2008;358:453-63

Chronic Effects of Neurotrauma Consortium



Site	Facility	Type	Study
Mid-Atlantic	Washington, DC VA Medical Center	★	1, 3
	Hunter Holmes McGuire VAMC, Richmond, VA	★▲	
	Walter Reed National Military Medical Center, Bethesda, MD	◆	
	Uniformed Services University, Bethesda, MD	◆	
	Virginia Commonwealth University, Richmond, VA	◆	
	Armed Forces Retirement Home, DC	▼	
Florida	James A. Haley Veterans' Hospital, Tampa	★▲	1, 4, 5
	University of South Florida, Tampa	◆	
	Reskamp Institute, Sarasota	■	

Site	Facility	Type	Study
Texas	Michael E. DeBakey VA Medical Center, Houston	★	1
	San Antonio Military Medical Center	◆	
	Brook Army Medical Center, San Antonio	◆	
	South Texas Veterans Health Care System, San Antonio	★▲	
	Baylor College of Medicine, Houston	◆	
Pacific Northwest	Puget South Healthcare System, Seattle	★	2, 4
	University of Washington, Seattle	◆	
California	San Francisco VA Medical Center	★	3, 4
	University of California, San Francisco	◆	
	Veterans Home of Yountville, CA	▼	
Chicago	Northwestern University, Chicago	◆	5
	Rush University Medical Center, Chicago	◆	

★ = VA medical centers; ▲ = DoD centers—DVBC; ◆ = DoD centers—MTF; ◆ = Academic universities; ▼ = Military retirement homes; ■ = Research Institutions; ● = Studies; — = Contributors to Studies; - - - = Veterans from Study 1 included in Study 2

Study Sponsors:

- Department of Defense (\$37.18 M)
- Veterans Administration (\$25 M)
- 2013 - 2018

Chronic Effects of Neurotrauma Consortium



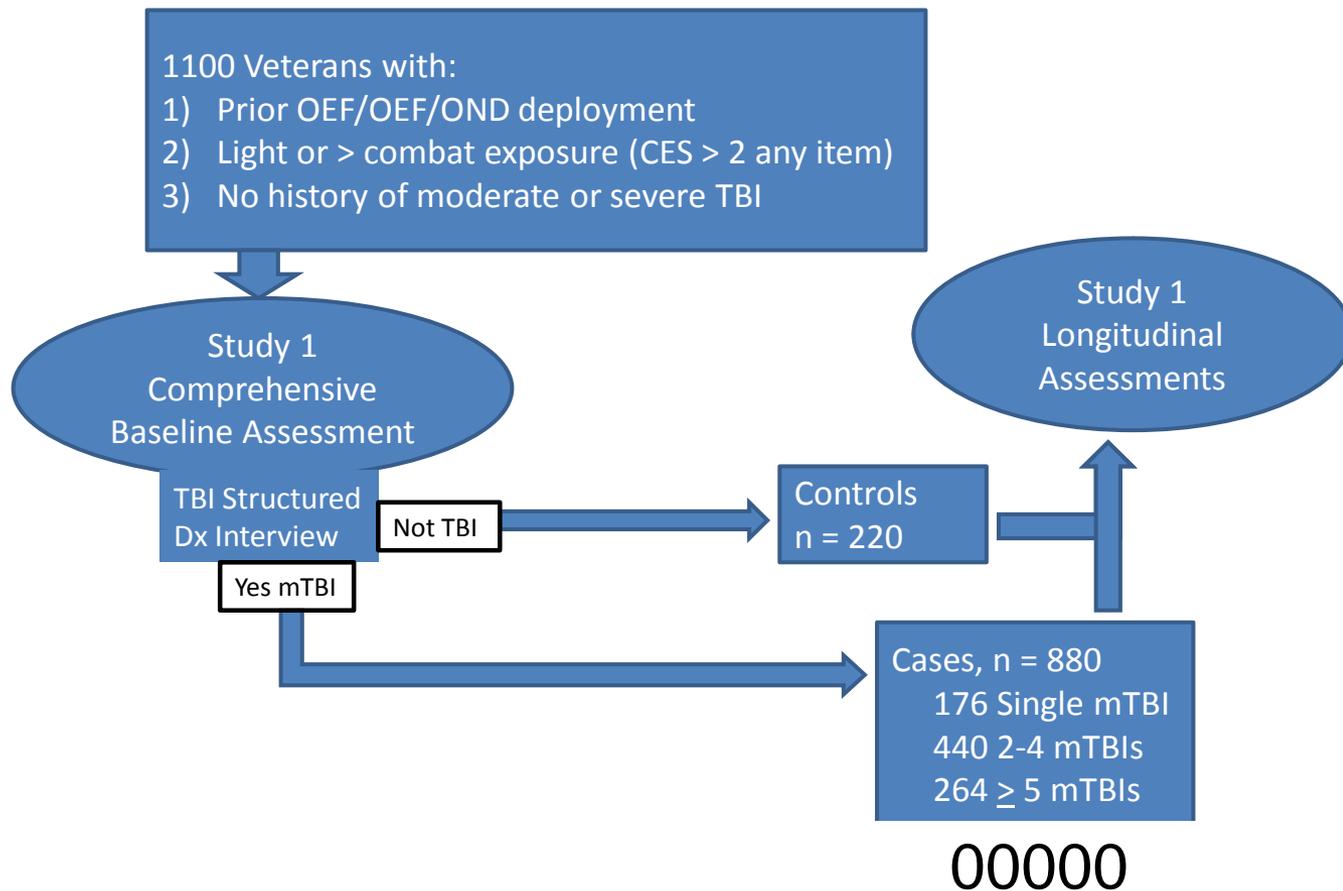
Projects

1. Longitudinal Cohort Study
2. Epidemiology Study
3. Tau Dysregulation Study
4. Otolith Organ Dysfunction
5. *Phase 2 clinical trial of Genotropin*
6. *Vestibular rehabilitation*

Cores

1. Data Management and Statistics Core
2. Biorepository Core
3. Neuroimaging Core
4. Neuropathology Core

Longitudinal Observational Study of Iraq/Afghanistan Veterans



Neuroimaging Core

Elisabeth Wilde, PhD

Harvey Levin, PhD

Getty York, MD

Erin Bigler, PhD

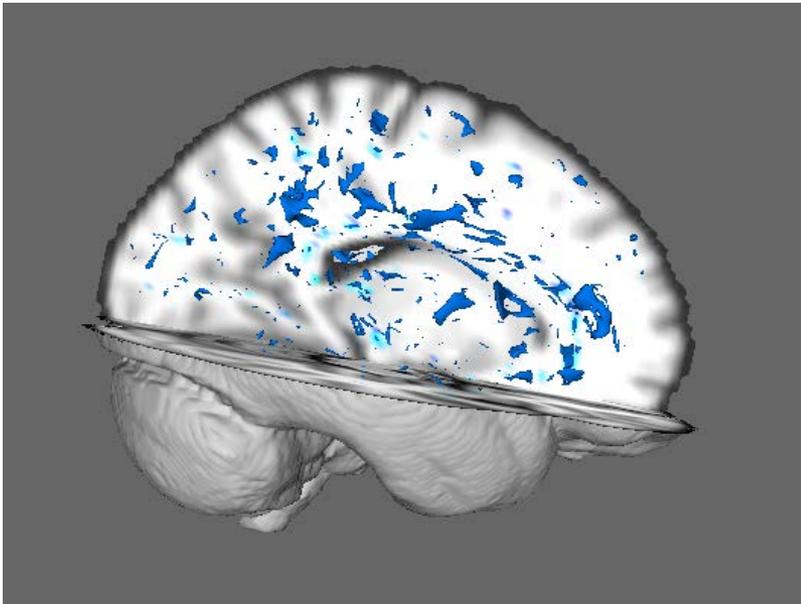


Figure 1. Results of the TBSS group analysis. Regions indicated in blue are areas of significant FA decrease in the group with blast-related mild TBI rendered on a three dimensional template (from L. Wilde, H. Levin, Baylor College of Medicine/Houston VAMC)

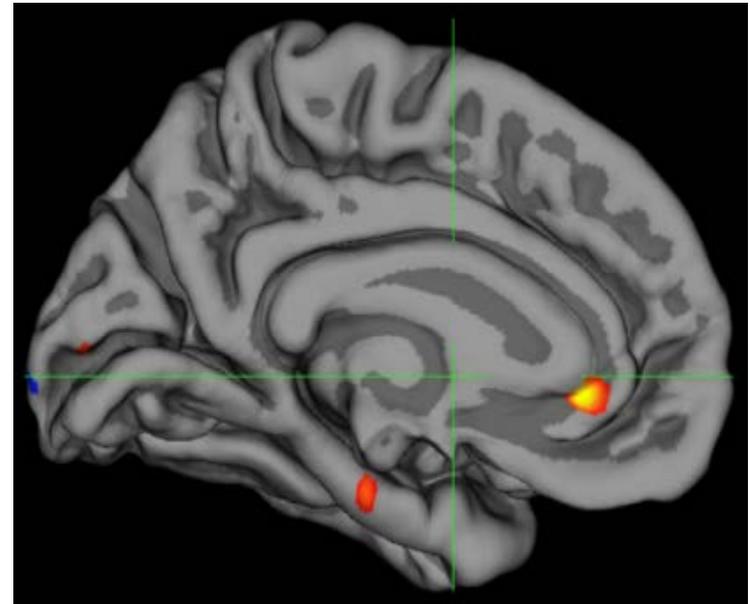
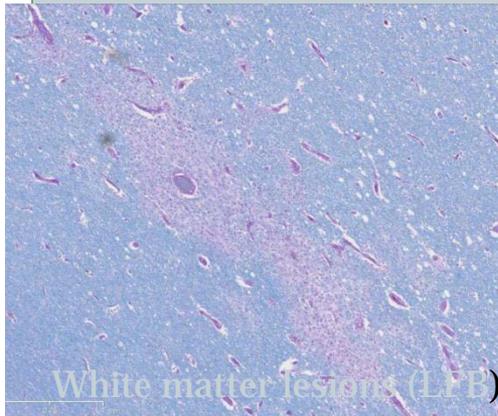


Figure 2: Colored regions indicate areas of significant cortical thinning in participants with TBI as compared to a control cohort. (from L. Wilde, H. Levin, Baylor College of Medicine/Houston VAMC)

Neuropathology Core

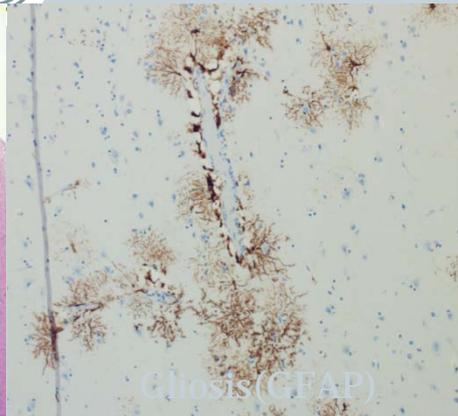
Dan Perl, MD



White matter lesions (LFB)



Contusion (H&E)



Gliosis (CFAP)



NFTs (Biels)

Calculation of Estimated Annual Specimen Accrual

Cohort	Age, years	Number in Cohort	Death Rate/1,000/yr (source)	Total Annual Deaths	Estimated % of deaths with brain donation	Estimated Brains Accessioned/year
Project 1	25-45	1,100 (over 4 years)	1.5/1000 (actuarial tables)	1	50%	0-1
Veterans from OIF/OEF/OND	20-35	1,800,000	1.5/1000 (actuarial tables)	2,700	1%	27
All Sources						45 specimens/year

Progress to date

TBI in the Modern Battlefield



Is it really
new?

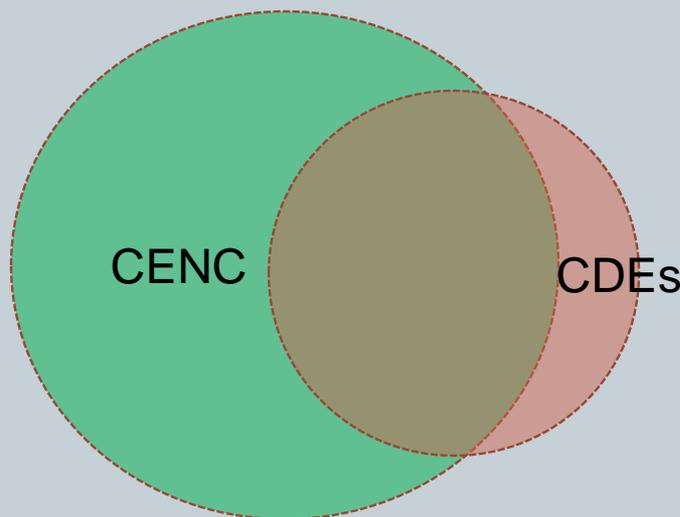


What percentage of your data is comprised of the International TBI Common Data Elements and what percentage are unique data elements?



- **For Longitudinal Study**

- >95% of demographic and injury characterization variables are from CDEs
- Many unique data elements for novel characterizations



- Neuroimaging, Biomarkers, Neuropathology >98% harmonized

Chronic Effects of Neurotrauma Consortium

- 
- Virginia Commonwealth University /Richmond VAMC
 - David Cifu
 - William Walker
 - Steve West
 - Uniformed Services University /CNRM
 - Ramon Diaz-Arrastia
 - Dan Perl
 - Brian Cox
 - Baylor College of Medicine /Houston VAMC
 - Harvey Levin
 - Elisabeth Wilde
 - Jose Garcia/Ricardo Jorge
 - Banner Neuroscience Institute
 - Elliott Mufson
 - UCSF /San Francisco VAMC
 - Kristine Yaffe
 - Deborah Barnes
 - University of Washington/Puget Sound VA
 - Nancy Temkin
 - Sureyya Dikmen
 - Christine MacDonald
 - University of South Florida /Tampa VAMC
 - Heather Belanger
 - Fiona Crawford
 - Mountain Home, TN VAMC
 - Faith Akin
 - RTI International
 - Rick Williams
 - Gayle Bieler
 - Doreen Collins