Development of a Biobehavioral-Based Machine Learning Model to Classify Subtypes of Mild Traumatic Brain Injury in Combat Veterans: A LIMBIC-CENC study

Jeffrey T. Howard[1], Allison Wright[2], Sara Mithani[3], Sandra Villegas Ibarra[1], Margaret Wells[2], Kirsten Verkamp[2], Alicia Swan[2]

[1] University of Texas at San Antonio, Department of Public Health [2] Polytrauma Rehabilitation Center, South Texas Veterans Health Care System

[3] University of Texas Health Houston, School of Nursing

Introduction

- Traumatic brain injury (TBI) is a major cause of death and disability.
- Treating TBI patients is challenging due to lack of precision in classifying severity and heterogeneity in symptoms and factors affecting outcomes Bazarian et al., 1999; Broshek et al., 2015; Lundin et al., 2006; McMahon et al., 2014; Snell 2010).

Objective: We aimed to develop a machine learning model to identify subtypes of mild TBI in a veteran cohort, which would be able to predict subsequent health outcomes, including mental health diagnoses, cardiovascular disease and diabetes.

Methods

Participants: Combat veterans (n=3,006) with a history of no more severe than mild TBI completed LIMBIC-CENC baseline and follow up visits.

Input Variables

- PHQ-9: Severity of depressive symptom burden.
- PCL-5: Severity of PTSD symptom burden.
- DRRI-2 Combat: Combat exposure during deployment.
- DRRI-2 Social Support: Perceived social support during deployment.
- PSQI: Sleep quality.
- AUDIT-C: Alcohol misuse.
- Demographics: Age, sex, race/ethnicity, education, marital status, and health insurance status.
- NSI: Neurobehavioral symptom burden
- TBI-QOL: Functioning, pain, anxiety, resilience, and social aspects of quality of life.
- Vital signs: BMI, blood pressure, heart rate
- Lab results: Testosterone, TSH, IGF-1
- Neuropsychological tests: Working memory, verbal memory, executive functioning, processing speed.
- Head Injury: Positive TBI exposure and post-concussive event exposure including blast.

Analysis:

- K-prototypes unsupervised clustering algorithm classified individuals into ***clusters*** using baseline sociodemographic and neurobehavioral data without considering specific outcomes.
- Elbow plot was used to determine final number of clusters.
- All analyses were run in R 4.4.2.

Results

Table 1. Sample Characteristics

Variable	Category	Total	p
Total N (%)		4867	
Period	Baseline	3006 (61.8)	0.003
	Follow-up 1	1462 (30.0)	
	Follow-up 2	399 (8.2)	
Age	Mean (SD)	44.2 (10.8)	<0.001
Sex	Female	611 (12.6)	<0.001
	Male	4251 (87.4)	
	Refused	3 (0.1)	
Race/Ethnicity	American Indian or Alaska Native	36 (0.7)	<0.001
	Asian	85 (1.7)	
	Black or African American	842 (17.3)	
	Hispanic	823 (16.9)	
	Other	79 (1.6)	
	Pacific Islander	32 (0.7)	
	White	2928 (60.2)	
	Donit know / Not sure	12 (0.2)	
	Refused	28 (0.6)	
	Missing	2 (0.0)	
Education	Grades 9 through 11 (Some high school)	9 (0.2)	<0.001
	Grade 12 or GED (High school graduate)	506 (10.4)	
	College 1 year to 3 years (Some college or technical school)	1792 (36.9)	
	College 4 years or more (College graduate)	2546 (52.5)	
Marital Status	A member of an unmarried couple	90 (1.9)	<0.001
	Married	2988 (61.6)	
	Never married	613 (12.6)	
	Separated	188 (3.9)	
	Divorced	928 (19.1)	
	Widowed	37 (0.8)	
	Refused	9 (0.2)	
Rank	Enlisted	2895 (85.0)	<0.001
	Officer	438 (12.9)	
	Warrant Officer	65 (1.9)	
	No Response	6 (0.2)	
Service Branch	Air Force	271 (8.0)	<0.001
	Air Force Reserves	52 (1.5)	
	Air National Guard	35 (1.0)	
	Army	1670 (49.1)	
	Army National Guard	333 (9.8)	
	Army Reserves	190 (5.6)	
	Coast Guard	4 (0.1)	
	Coast Guard Reserves	3 (0.1)	
	International Guard	2 (0.1)	
	Marine Corps	466 (13.7)	
	Marine Corps Reserves	37 (1.1)	
	Navy	319 (9.4)	
	Navy Reserves	22 (0.6)	
Number of TBIs	Mean (SD)	1.3 (1.8)	0.786

Figure 2. Elbow Plot

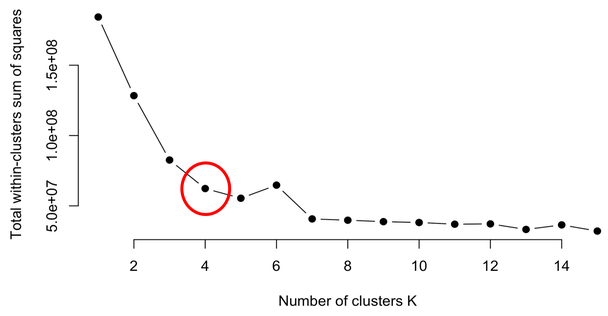


Figure 1. Unsupervised Learning with k-prototypes Algorithm

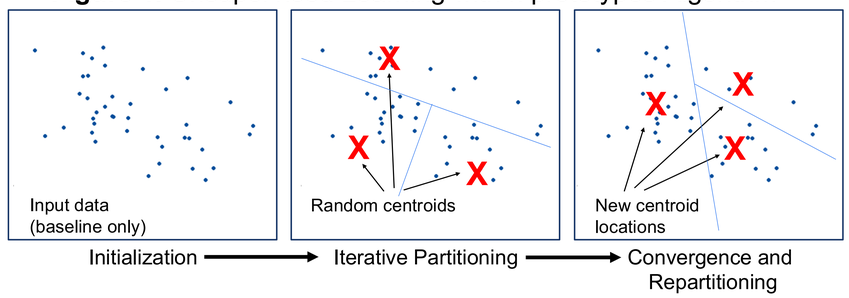


Figure 3. Heatmap of Key Variables by Cluster

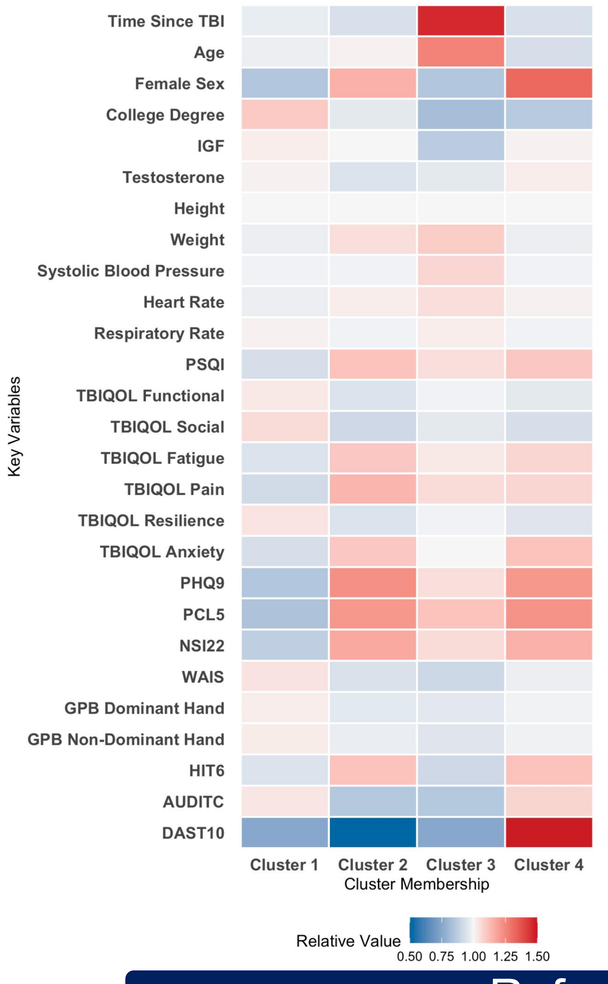
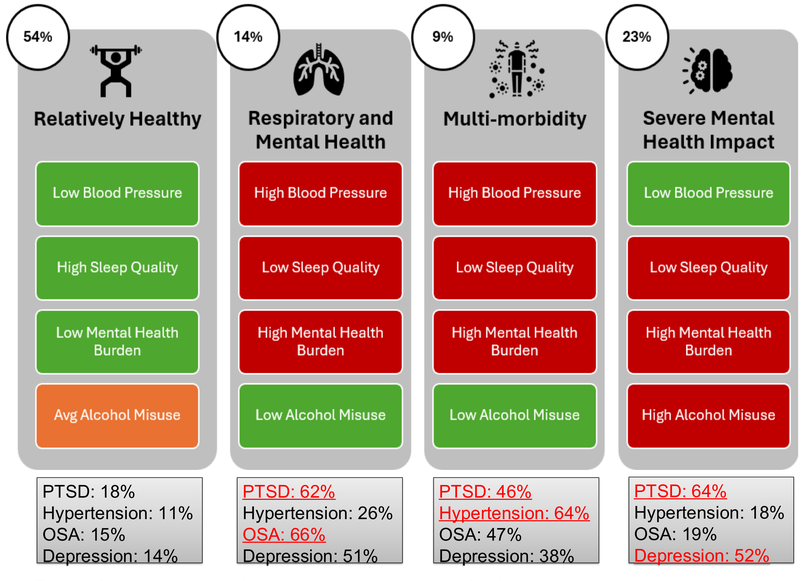


Figure 4. Cluster Descriptions and Clinical Profiles



* Example diagnosis incidence percentages by cluster

Summary

- Clusters identified were similar to phenotypes found in prior studies:
  - "Healthy"
  - "Mental Health Burden"
  - "Multimorbidity"
- Clinical implications and utility:
  - Enhance detection of comorbidity patterns common after mild TBI
  - Facilitates identifying risk for adverse outcomes like depression, PTSD, suicide, substance use, cardiovascular disease and diabetes
  - Facilitates patient-centered care by revealing likely comorbidity patterns and enabling strategic care provision

What's new?

- Cluster membership predicted multiple outcomes despite not including any outcomes in the initial algorithm to identify clusters.
- Mental Health conditions were common among all but the 'Relatively Healthy' group; subtypes varied in comorbidity presentation
  - *Severe MH burden (e.g., PTSD, Depression)*
  - *Multimorbidity (e.g., Hypertension, Diabetes)*
  - *Respiratory & MH (e.g., OSA)*

Limitations

- Self-report data
- Specificity to the leveraged, clinically rich, dataset

Future Research

- Applying this model to identify mild TBI clusters may improve healthcare providers' capacity to detect and intervene health risks at an earlier stage.
- Further research should seek to validate risk prediction with longitudinal data.
  - Tracking outcomes compared to predicted risk models
  - Conducting the same algorithm with longitudinal data to track changes in cluster identification and membership

Funding

Funded by the San Antonio Medical Foundation FY24 Collaborative Grant awardee (PI Howard [UTSA]; co-I Swan [STVHCS]; co-I Mithani [UTHouston]).

References

- Bazarian, J. J., Wong, T., Harris, M., Leahey, N., Mookerjee, S., & Dombovy, M. (1999). Epidemiology and predictors of post-concussive syndrome after minor head injury in an emergency population. Brain injury, 13(3), 173-189.
- Broshek, D. K., De Marco, A. P., & Freeman, J. R. (2015). A review of post-concussion syndrome and psychological factors associated with concussion. Brain injury, 29(2), 228-237.
- Lundin, A., de Boussard, C., Edman, G., & Borg, J. (2006). Symptoms and disability until 3 months after mild TBI. Brain injury, 20(8), 799-806.
- McMahon, P. J., Hricik, A., Yue, J. K., Puccio, A. M., Inoue, T., Lingsma, H. F., ... & Vassar, M. J. (2014). Symptomatology and functional outcome in mild traumatic brain injury: results from the prospective TRACK-TBI study. Journal of neurotrauma, 31(1), 26-33.
- Snell, F. I., & Halter, M. J. (2010). A signature wound of war: mild traumatic brain injury. Journal of psychosocial nursing and mental health services, 48(2), 22-28.