

Personal Perspectives of Allostatic Load as Modifiers of Functional Recovery in Two Cohorts with TBI: A NEXUS Study

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Introduction

- Traumatic brain injury (TBI) is recognized as a chronic condition that can lead to lasting impairment across the injury severity spectrum.
- Allostatic load (AlloL),¹ the cumulative burden of stress exposure manifested in physiological, psychological, &/or behavioral symptoms, has historically been measured only with molecular biomarkers
- Capturing multi-domain AL indicators in the TBI context may offer unique insight into contextualizing modifiers that impact TBI recovery trajectories
- This complements the CBIM approach to TBI classification^{2,3}: Clinical Assessment (i.e. Glasgow Coma Scale) Blood-based Biomarkers Imaging, Modifiers (i.e. personal factors, mental health, medical history, co-morbidity, environmental factors)

Objective

To qualitatively assess the impact of AlloL and its unique modifiers that shape recovery after TBI, we recruited individuals with lived experience of TBI to share their experience of the challenges associated with recovery

Materials and Methods

- Two community engagement studios (CES)—structured, group discussions facilitated by a study investigator
- Recruitment from two longitudinal cohorts of TBI related injuries—one mild and one moderate-to-severe: First group - 9 mTBI participants; Second group - 3 msTBI participants and 4 caregivers (CG)
- Each CES presented participants with a definition & examples of AlloL.
- Sessions were held virtually via Zoom and were recorded

Analysis

Participants responded to two questions:

1. Think about the domains of AlloL that we have described, which have had the greatest impact on you?
2. Describe how the “load” that you have built up has impacted your brain injury and your recovery?

Artificial intelligence ([AI] Anthropic, Claude Sonnet 4.6) tool was prompted to generate an informal thematic analysis. Prior to feeding the deidentified transcripts, the AI was prompted to construct the codebook of domains and sub-codes based on a definition of AlloL.

This process was used for informal exploratory analysis; findings were not subjected to inter-rater reliability procedures. Data from both studies were combined for analysis—but group specific comparisons were also completed.

Results

AI identified 7 domains and 29 sub-codes and reviewed by investigators (JD, MLP, AKW).

Figure 1. Frequency of AlloL concepts Combined (N=16)



Discussion

- The data we collected through the studios support the personal “modifiers” approach to injury diagnosis, prognosis, and treatment planning
- Including questionnaires and assessment tools to capture AlloL in the acute and chronic phases after TBI would help to identify and characterize modifying factors that impact recovery
- This approach represents a multi-domain, precision medicine approach to TBI’s chronic disease state
- Some of the participation in the second group with msTBI participants relied on CGs because of the inability of the participants to communicate—however, we took this approach to ensure we captured the CG perspective and obtain an albeit indirect perspective from those with the most severe injuries.

Impact

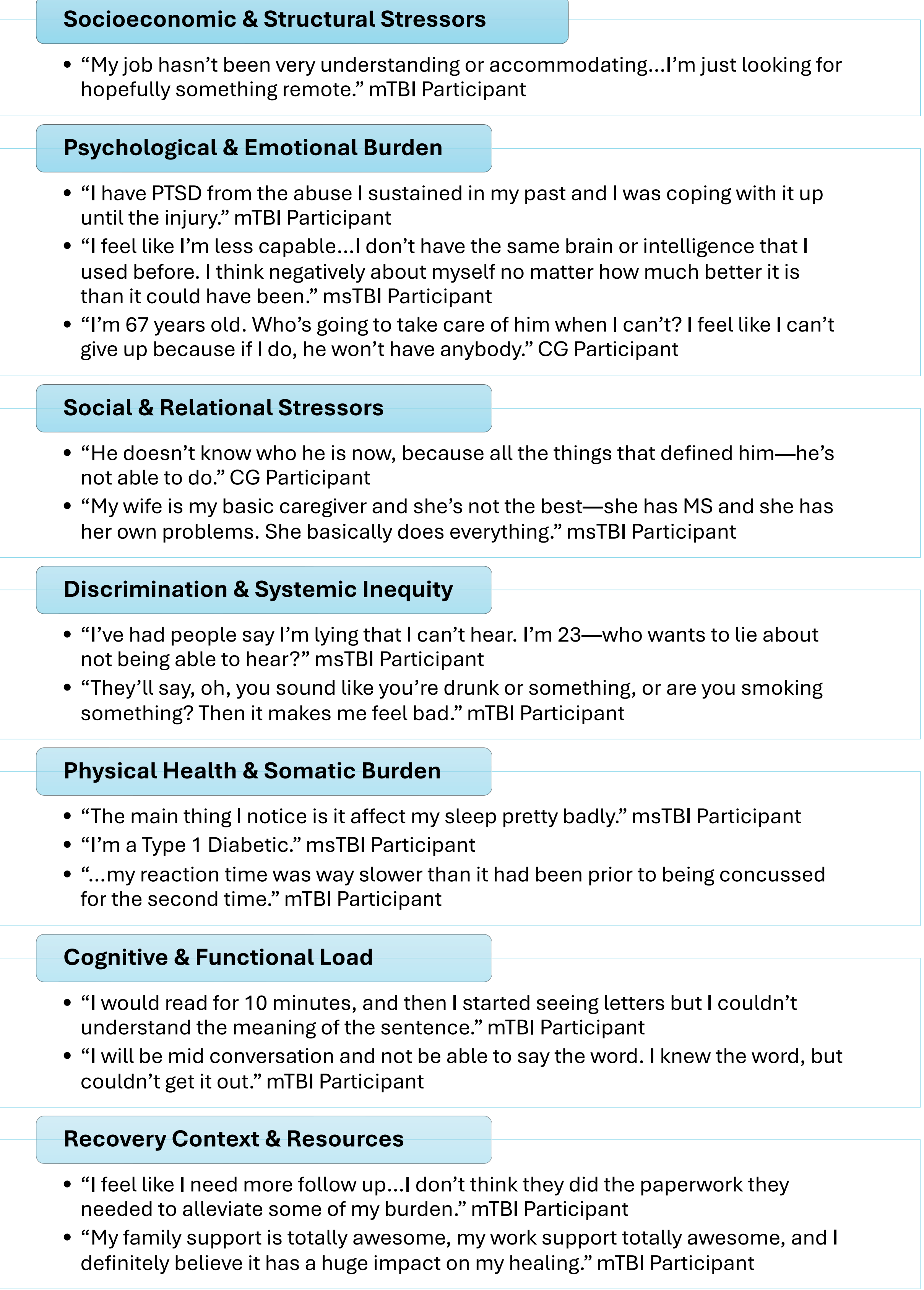
Qualitative data on the multi-layered impacts of AlloL on TBI recovery highlight crucial factors to consider in addition to traditional injury severity metrics when considering TBI recovery trajectories. Findings are consistent with the multidimensional framework of CBIM and supported by the WHO International Classification of Functioning, Disease & Health. Including AlloL measures into the CBIM framework may further enhance the utility of this framework in understanding recovery trajectories across the injury severity spectrum

Future Steps

- On-going efforts to conduct two more studios with participants from both groups (mTBI and msTBI / CG) to increase our dataset for a more formalized analysis
- Continue collecting longitudinal data that integrates AlloL into clinical decision-making

References: 1. McEwen BS. Stress, adaptation, and disease. Allostasis and allostatic load. Ann N Y Acad Sci. 1998;840:33-44. doi: 10.1111/j.1749-6632.1998.tb09546.x. 2. New Framework for Classifying Traumatic Brain Injury (TBI) Could Transform Patient Care. Director's Message [Internet]. 2025 29 May 2026. Available from: <https://www.ninds.nih.gov/news-events/directors-messages/all-directors-messages/new-framework-classifying-traumatic-brain-injury-tbi-could-transform-patient-care>. 3. Manley GT, Dams-O'Connor K, Alosco ML, Awwad HO, et. al. A new characterisation of acute traumatic brain injury: the NIH-NINDS TBI Classification and Nomenclature Initiative. The Lancet Neurology. 2025;24(6):512-23. doi: 10.1016/S1474-4422(25)00154-1.

Figure 2. Illustrative quotes



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