Neuroinflammatory biomarkers, symptoms, and functional outcomes in individuals with moderate traumatic brain injury

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Purpose/Specific Aims:

Traumatic brain injury (TBI) is a significant public health concern and little is known about the relationship between symptoms and functional outcomes in this population. Furthermore, there are no established biomarkers to objectively monitor, predict, or aid in prescribing interventions, especially for moderate TBI which is understudied compared to mild and severe TBI. This study seeks to address these gaps by first understanding the symptom experience of individuals with moderate TBI during the convalescence period, and assess the moderating effect of neuroinflammatory biomarkers on the relationship between symptoms and functional outcomes. The specific aims are:

Aim 1 (Primary): Characterize the physical, cognitive, and affective symptoms (both frequency and severity) in individuals with moderate TBI (3-12 mo. Post-TBI)

Aim 2 (Secondary): Examine the relationship between symptom frequency/severity and functional outcomes (disability, QoL) among individuals with moderate TBI (3-12 mo. Post-TBI)

Aim 3 (Exploratory): Examine the extent that neuroinflammatory biomarkers (IL-6, S-100ß, RAGE, GFAP) moderate the relationship between symptoms and functional outcomes in individuals with moderate TBI (3-12 mo. Post-TBI).

Rationale/Significance of Study:

Little is known about the symptoms experienced during recovering from a moderate TBI, that is, the post-acute period. Additionally, TBI remains a poorly understood clinical phenomena, as some patients are able to fully recover, while others have long lasting, persistent symptoms. The importance of symptoms is highlighted from the numerous studies illustrating the negative impact they have on recovery and quality of life across diseases and populations. We hypothesize that symptoms experienced by those with a moderate TBI may be attributable to underlying neuroinflammation, which may be more pronounced in some patients; however, research is sparse in this area.

Conceptual or Theoretical Framework:

The following theoretical framework will be used.

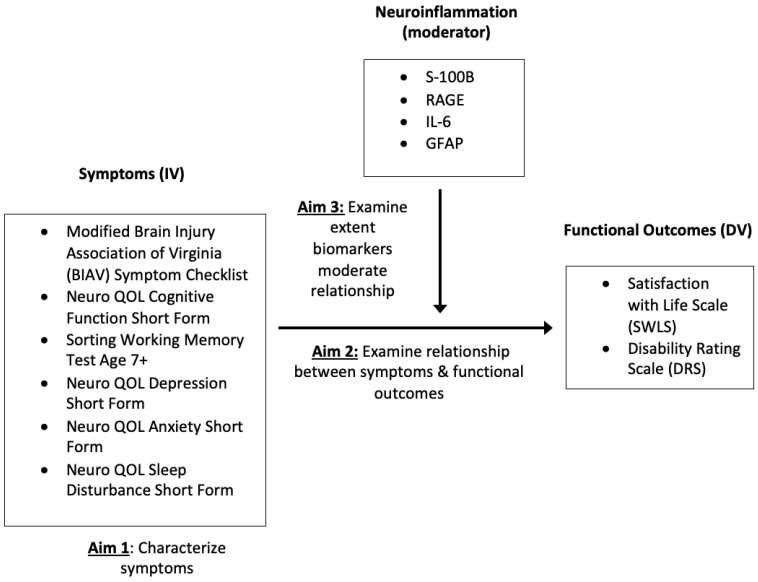

Figure 2

Main Research Variables:

This study will examine the moderating effect of the biomarkers S-100ß, RAGE, GFAP, and IL-6 (moderators) on the relationship between symptoms (independent variable) and functional outcomes (dependent variable). Symptoms examined will include: cognitive function, working memory, depression, anxiety, and sleep, in addition to a general Symptom Checklist; functional outcomes examined will include satisfaction with life and functional ability.

Design:

This is a descriptive, cross-sectional study.

Setting:

This study will be conducted at the TBI clinics at Jackson Memorial Hospital, a 1500 bed Level 1 Trauma Center, in Miami, Florida. The TBI clinics serve over 500 patients each year with 35% having sustained moderate TBI.

Sample:

125 participants will be required for this study. Inclusion criteria include patients 3-12 months post moderate TBI (GCS 9-12), are age 18 years or older, capable of providing informed consent (assessed by MacArthur Competence Assessment), and speak English or Spanish. Individuals with a history of stroke, documented cognitive impairment, Major Depressive Disorder or Generalized Anxiety Disorder prior to sustaining the TBI will be excluded.

Methods:

Symptoms and functional outcomes will be assessed by administering electronic self-report measures to participants. This includes a general Symptom Checklist and 5 focused symptom assessments (2 cognitive and 3 affective), as well as 2 functional outcome assessments. Additionally, the biomarkers S-100ß, RAGE, GFAP, and IL-6 will be assessed by obtaining a blood sample from participants. Statistical analysis will include characterizing symptoms using descriptive statistics, T-tests, and chi-square tests to compare between ages 18-29 and ages 30+ (aim 1); constructing 2 linear regression models to examine the relationship between symptom severity/frequency and functional outcomes, while stratifying by age 18-29 and 30+ (aim 2); and constructing a moderation model to examine the influence of the biomarkers on this relationship (aim 3).

Implications for Trauma Nursing Practice:

Obtaining a greater understanding of the symptom experience of TBI patients in the post-acute/convalescence period will enable nurses and clinicians to develop and tailor interventions to maximize recovery from TBI. Moreover, this study will provide needed insight into the physiology underpinning recovery from TBI, as well as potential links between biomarkers and symptoms in those with TBI. This would lay the critical foundation needed for validation and use of biomarkers to predict and monitor the emergence or change in symptoms that could be used to guide clinical care.