

Era Veterans with Traumatic Brain Injury and/or Post-Traumatic Stress Disorder: A Department of Defense Alzheimer's Disease Initiative (DoD-ADNI) Study

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Objective: Research indicates that Veterans with a history of traumatic brain injury (TBI) are at increased risk for dementia. Although the precise mechanisms underlying this relationship are poorly understood, remote TBI may exacerbate normal age-related changes to cerebral white matter (WM) and result in cognitive decline. However, Veterans commonly experience a constellation of mental (e.g., post-traumatic stress disorder [PTSD] and depression) and vascular (e.g., diabetes, hypertension, obesity) health conditions that have also been implicated in pathologic cerebral WM and cognitive aging trajectories. Therefore, the present study sought to (1) clarify the effects of remote TBI within the context of PTSD, depression, and vascular risk on WM micro- and macrostructure, and (2) explore if WM integrity is associated with cognition in a sample of Vietnam-Era Veterans.

Participants and Methods: The sample consisted of 195 male Veterans ages 60-80 (mean age=69.3) enrolled in the Department of Defense-Alzheimer's Disease Neuroimaging Initiative (DoD-ADNI) study. 102 Veterans met criteria for TBI by sustaining a head-injury that resulted in a loss of consciousness, alteration of consciousness, or post-traumatic amnesia. Current and/or lifetime PTSD was designated by scores ≥ 30 on the Clinician-Administered PTSD Scale. The Geriatric Depression Scale was used as a continuous measure of depression. A vascular risk score (0-3) was calculated based on diabetes, hypertension, and obesity (BMI ≥ 30 kg/m²). An executive functioning composite was created by averaging sample-specific z-scores for Trail Making Tests (A and B), with higher scores indicating worse performance. Voxelwise analysis of WM microstructure (fractional anisotropy [FA]) was conducted with Tract-Based Spatial Statistics (TBSS), using non-parametric permutation testing with threshold-free cluster enhancement. SPM's Lesion Segmentation Tool was used to investigate WM macrostructure (WM hyperintensity [WMH]

volume). Lesion probability maps were masked to restrict WMH volume calculations to WM. Robust regression using M-estimation and predictive R² calculated using 10-fold cross-validation examined WMH volume, predictor, and cognitive associations. Age was a covariate in all WM analyses, and education was a covariate in all cognitive analyses.

Results: TBSS analysis revealed widespread, significant negative relationships between vascular risk and FA across numerous WM tracts (p 's ≤ 0.05). These associations remained significant after adjusting for TBI history, PTSD, and depression. TBSS identified significant positive relationships between executive functioning performance and FA across similar brain regions (p 's ≤ 0.05). Robust regressions revealed that vascular risk significantly predicted WMH volume ($p=0.006$; $\beta=0.161$; $R^2=0.093$), whereas TBI history, PTSD, and depression did not (p 's=0.107-0.166; β 's=-0.089-0.101). WMH volume significantly predicted executive functioning ($p=0.002$; $\beta=0.216$; $R^2=0.105$), whereas TBI history, PTSD, depression, and vascular risk did not (p 's=0.123-0.888; β 's=-0.012-0.125).

Conclusions: Our results suggest that vascular health, relative to remote TBI, PTSD, and depression, may be more robustly associated with cerebral WM micro- and macrostructure in older Veterans. Furthermore, poorer WM integrity is associated with poorer cognitive performance. These findings underscore the importance of vascular health interventions in preventing negative brain and cognitive aging outcomes in Veterans, independent of TBI history. Future studies might leverage other neuroimaging modalities (e.g., functional MRI) to further investigate the effects of vascular health on aging in Veterans with a history of TBI.

Categories: Acquired Brain Injury (TBI/Cerebrovascular Injury & Disease - Adult)

Keyword 1: traumatic brain injury

Keyword 2: aging (normal)

Keyword 3: neuroimaging: structural connectivity

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19 Impact of Rehabilitation Pathway on the Prediction of Social Participation

Outcome and Productivity After Traumatic Brain Injury

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Objective: Social participation (SP) represents a key goal in TBI rehabilitation, as it allows the individual to return to active and purposeful roles in the community. However, studies on predictors of SP specific to post-acute universally accessible specialized rehabilitation pathways following TBI are scarce. Our objectives were thus to 1) characterize a literature-based set of pre-injury, injury-related, and post-injury variables, as well as SP (measured with the MPAI-4 Participation scale) in individuals participating in inpatient-outpatient or outpatient rehabilitation pathways within a universally accessible and organized trauma continuum of care and 2) assess the use of these variables to predict SP outcome after TBI for each rehabilitation pathway.

Participants and Methods: Participants ($N = 372$) were adults admitted between 2016 and 2020 to an inpatient-outpatient rehabilitation pathway or an outpatient rehabilitation pathway after sustaining a mild, moderate or severe TBI. The French-Canadian adaptation of the MPAI-4 questionnaire (Malec, 2005; Guerrette & McKerral, 2021; McKerral et al., 2014) presents three subscales (Abilities, Adjustment, Participation) and a total score, assessing functional and SP outcome after TBI. The MPAI-4 is completed for all individuals at admission and discharge in three major rehabilitation centers in the greater Montreal region. Independent variables consisted of sociodemographic and clinical characteristics collected from medical files and rehabilitation databases. Outcome measures consisted of a general SP level (MPAI-4 Participation subscale score at discharge from outpatient rehabilitation) and productivity status at discharge (productive if employed, child rearing, homemaker, student or volunteering; unproductive if unemployed or retired). Multiple and logistic regressions investigated the predictive value of each variable for SP outcome and productivity, separately for each rehabilitation pathway.

Results: Samples' sociodemographic and clinical characteristics differed between

rehabilitation pathways. The inpatient-outpatient sample presented older age, lower productivity before TBI and poorer SP levels at admission and discharge from rehabilitation. However, both samples showed significant improvement on SP levels during rehabilitation. For the inpatient-outpatient rehabilitation path, general SP outcome was significantly predicted by three variables (education years, MPAI-4 Ability and Adjustment scores at rehabilitation intake; $R^2 = 49\%$), whereas productivity status at discharge was significantly predicted by age at time of injury ($R^2 = 72\%$). For the outpatient rehabilitation path, general SP outcome was significantly predicted by five variables: premorbid hypertension, mental health diagnosis, total indirect rehabilitation hours received, MPAI-4 Abilities and Adjustment scores at rehabilitation intake ($R^2 = 47\%$), while productivity status at discharge was significantly predicted by age at time of injury and education years ($R^2 = 44\%$).

Conclusions: Different TBI rehabilitation care pathways showed distinct sample characteristics, as well as different premorbid and post-injury predictors of SP outcome and productivity. This highlights the importance of being aware of the potential limited generalizability of previously identified predictors when extrapolated to different clinical, rehabilitation and sociocultural contexts. The predictive models obtained could help clinicians identify more accurately patients at risk of showing poorer SP and productivity outcomes at end of rehabilitation, influence intervention approaches put forward with these individuals and set more appropriate goals and expectations.

Categories: Acquired Brain Injury (TBI/Cerebrovascular Injury & Disease - Adult)

Keyword 1: traumatic brain injury

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20 The Influence of Brain Injury Severity, Anxiety, and Depression on Objective and Subjective Prospective Memory Problems