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The unique contribution of fatigue to disability in community dwelling adults with traumatic brain injury

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Abstract

Objective—To examine the unique contribution of fatigue to self-reported disability in community dwelling adults with traumatic brain injury (TBI).

Design—A cross-sectional cohort design.

Setting—Community dwellings in the greater Pittsburgh region.

Participants—Fifty adults with a history of mild to severe TBI were assessed.

Main Outcome Measure—This study assessed the contribution of fatigue (Modified Fatigue Impact Scale) to disability (Mayo Portland Adaptability Inventory IV), controlling for executive functions (Frontal Systems Behavior Scale), depression status (major depression in partial remission/current major depression/depressive symptoms or no history of depression), and initial injury severity (uncomplicated mild, complicated mild, moderate, or severe).

Results—Fatigue was found to contribute uniquely to the variance in self-reported disability ($\beta=.47$, $P<0.001$) after controlling for injury severity, executive functions, and depression status. The overall model was significant ($F_{4,45}=17.32$, $P<.001$) and explained 61% of the variance in self-reported disability, with fatigue alone accounting for 12% of the variance in self-reported disability ($F_{1,45}=13.97$, $P<.001$).

Conclusions—Fatigue contributes uniquely to disability status among community-dwelling adults with chronic TBI, independently of injury severity, executive functions, and depression. Addressing fatigue through targeted interventions may help to improve self-perceived disability in this population.

Keywords

Brain Injuries; Fatigue; Rehabilitation

The goal of rehabilitation is to minimize disability and maximize independence for individuals with disabilities. To achieve this goal, rehabilitation professionals implement interventions developed from best evidence and directed at significant factors contributing to disability. Among adults with traumatic brain injury (TBI), there are a multitude of factors that contribute to long term disability, including impaired cognition, behavioral changes,

depression, and fatigue.(1–7) Among these factors, many individuals with TBI endorse fatigue as their most distressing and challenging symptom, even among those with mild injuries.(8) Approximately 50–80% of individuals with TBI experience significant fatigue that contributes to disability.(2, 3, 9–14) Fatigue experienced by individuals with TBI does not resolve spontaneously and is chronic in nature, negatively influencing social, physical, and cognitive functioning.(15–19), Reports differ on how fatigue influences participation, indicating that fatigue may or may not results in decreased quality of participation in everyday life and increased work disability.(11, 20–22) Depression and cognitive impairment, two factors highly associated with fatigue after TBI(10, 23–25) also contribute to disability.(23, 26–28) While fatigue has been shown to be a sequela of TBI that is distinct from depression and cognitive impairment,(10, 15) it is unknown how fatigue independently contributes to disability after TBI. To address this question, the goal of the current study was to examine whether fatigue uniquely contributes to disability in community-dwelling adults with TBI, after controlling for injury severity, executive functions, and depression status. A further exploratory aim was to examine the same question in a subgroup of participants experiencing significant fatigue.

Method

Design

This study used a cross-sectional cohort design of adults with mild to severe traumatic brain injury living in a community setting. This was a secondary analysis of an existing dataset.

Participants

Individuals were recruited through a university-affiliated medical center, and all research was approved by the University's Institutional Review Board (IRB#PRO11030543). The purpose of the parent study, as explained to participants, was to explore factors associated with participation outcomes among community-dwelling adults with a history of TBI. Inclusion criteria were as follows: 1) adults with a history of mild to severe TBI; 2) at least 6 months post injury, 3) living in a private or group residence in the community. Mild to severe TBI was defined as any injury sustained from an outside force to the head resulting in an initial Glasgow Coma Scale (GCS) score of 3–15 with positive neuroradiologic findings (or in cases where investigators did not have access to medical records, sufficient functional compromise to be eligible for ongoing services requiring evidence of TBI diagnosis).(29) Exclusion criteria were: 1) any history of a condition resulting in progressive cognitive decline (e.g. dementia); 2) current active (untreated) psychotic or bipolar disorder; 3) current involvement in injury-related litigation.

Eighty-seven individuals responded to recruitment letters, advertisements, and outreach activities for the parent study. Upon initial phone screening, 16 were not interested in research, 4 did not meet injury severity criteria, 2 were currently involved in injury-related litigation, 1 passed away prior to scheduling a visit, and 2 had not been screened at the time of these analyses. Sixty-two individuals met initial screening criteria and 60 provided written informed consent. After consent, additional screening was conducted to determine eligibility. This screening process involved review of medical records to determine injury severity, review of demographic information, and completion of the Mood PRIME-MD(30) to determine current mental health status. As a result of additional screening, 2 individuals were determined to be ineligible due to active untreated bipolar disorder with psychotic features and three did not meet injury severity criteria after review of medical records. Thus, 55 individuals were deemed eligible to participate in the parent study. Subsequently for these analyses, 5 individuals were excluded due to failure to complete all assessments.

Therefore, 50 individuals completed all study assessments and were included in the present analyses.

Measures

At the time of assessment, demographic data was collected, including age, gender, race, years of education, and history of inpatient rehabilitation. In addition, descriptive data including time since injury, injury severity, disability, fatigue, executive functions, depression status, self awareness, and cognitive functioning were also collected.

Injury Severity was measured by the GCS at the time of initial injury. Consistent with previously described definitions, participants were categorized as having had an uncomplicated mild (GCS 13–15 with enough functional compromise to ongoing services) (31), a complicated mild (GCS 13–15 with positive neuroradiologic findings), amoderate (GCS 9–12), or a severe (GCS 8) injury(29).

Disability was assessed with the Mayo Portland Adaptability Inventory (MPAI).(32, 33) Each of the 25 items on the MPAI is rated on a 0–4 scale, with 0 indicating no problem and 4 indicating a severe problem that interferes with activities more than 75% of the time. A total self reported score (range 0–100) is calculated and converted into a *T-score* derived specifically for the TBI population, with higher *T-scores* indicating more severe disability. (33)

Fatigue was assessed with the modified Fatigue Impact Scale (mFIS), a general scale that measures the impact of fatigue on everyday life in 3 dimensions – Cognitive, Physical, and Psychosocial(34) - and has been validated in a TBI population.(13) The mFIS includes 21 items each rated on a 5-point ordinal scale ranging from 0 (no problem) to 4 (extreme problem). A total summed score is derived, ranging from 0–84, with higher scores indicating greater fatigue. A cut point of total scores greater than 38 indicating clinically significant fatigue has been previously established in a population of adults with multiple sclerosis.(35)

Executive Functions were assessed with the Self-Report version of the Frontal Systems Behavior Scale (FrSBe), a 46 item tool that assesses behaviors associated with damage to frontal systems and serves as a measure of executive functions in daily life.(36) This scale has been validated in the TBI population when completed as a self-report and yields a total score (range 0–230) that is converted to a *T-score* adjusted for age, gender, and education, with higher *T-scores* indicating greater executive impairment.

Depression Status was assessed with the PRIME-MD, a diagnostic interview that assesses current and history of major depressive disorder and mania(30). Based on responses, participants were classified as having current depression/depressive symptoms, having history of depression/depression in partial remission, or having no history of depression. No statistically significant differences were found between those with a history of depression/depression in partial remission and those with current depression/depressive symptoms for any of the independent variables in this study. Therefore, depression status was dichotomized into two groups: those with no history of major depressive disorder and those with history of depression/depression in partial remission or current depression/depressive symptoms.

Self Awareness was measured with the Self Awareness of Deficits Interview (SADI). Self awareness was assessed because all measures in this study relied on self report. The SADI consists of a structured interview with questions designed to capture three components of self awareness: awareness of deficits, awareness of functional implications of deficits, and setting realistic goals. Each of these three components is rated on a scale from no disorder of

self awareness (0) to severe disorder of self awareness (3). Individual component scores are then summed to produce a total score (ranging from 0–9), with higher scores indicating greater impairment in self awareness.(37) Scores were based on a clinician interview and observation, as well as interview with a family member or significant other.

Analyses

Data were entered and analyzed using SPSS19.0 for Windows. We examined descriptive statistics for all of the variables, followed by Pearson correlations among the primary variables of interest. We then conducted two consecutive multiple linear regressions to test our hypothesis that fatigue would independently contribute to disability after controlling for injury severity, executive functions, and depression status, and to assess the magnitude of this contribution. The first model (Model 1) included only the covariates: injury severity, executive functions, and depression status. The second regression added fatigue to the model (Model 2). The change in the R^2 value between these two models represents the individual contribution of fatigue to disability, after controlling for the other covariates. Model diagnostics were assessed to assure good fit for the model, including variance inflation factor and tolerance.

An exploratory subgroup analysis was also performed to assess our hypothesis only for participants reporting clinically significant fatigue. For this analysis, participants were included if their mFIS scores exceeded the cut point of a total score >38, as established previously in the literature. Descriptive statistics were examined for this subgroup and the two consecutive linear regressions were performed according to the same procedure described above.

Results

Descriptive

The descriptive data for this study are summarized in Table 1. Overall, study participants ($n=50$) reported a mean standardized disability score within an average range for individuals with TBI, with a trend towards less than average disability ($M=44.02$, $SD=13.7$), and a mean standardized FrSBe score indicating impaired executive functions ($M=64.28$, $SD=21.8$). On average, study participants reported a level of fatigue ($M=36.06$, $SD=20.7$) comparable to individuals with multiple sclerosis known to be experiencing clinically significant disease-related fatigue.(35, 38) Finally, participants overall demonstrated good self awareness ($M=1.66$, $SD=2.16$).

Correlations

Pearson Correlations were completed to determine associations among the primary variables of interest. Results of these correlations are summarized in Table 2. Disability was significantly correlated with fatigue ($r=.679$, $P<.001$), injury severity ($r=.263$, $P=.032$), executive functions ($r=.599$, $P<.001$), and depression status ($r=-.511$, $P<.001$), as expected.

Regressions

Results of the regression analyses are presented in Table 3. Overall, fatigue, injury severity, executive functions, and depression status together explained 61% of the variance in disability among adults with TBI ($F_{4,45}=17.32$, $P<.001$). Of this 61%, fatigue alone accounted for 12% of the variance in disability ($F_{1,45}\Delta=13.97$, $P=.001$) based on the change in the R^2 value from Model 1 (without fatigue as a covariate) to Model 2 (with fatigue as a covariate).

Based on the standardized betas in Model 2, fatigue ($\beta=.47$) was the strongest predictor of disability relative to the covariates in the model ($\beta=.09-.28$). When added in Model 2, fatigue became the strongest predictor of disability, whereas impaired executive functions were the strongest predictor in Model 1. Depression status was no longer a statistically significant independent predictor of disability after fatigue was added to the model.

Model diagnostics indicated an overall good fit for the model. The variance inflation factor ranged from 1.03 to 1.82 and the tolerance ranged from .55 to .97, indicating no collinearity among predictors.

Subgroup Analysis

The descriptive data for this subgroup are presented in Table 1. The purpose of this subgroup analysis was to explore the unique contribution of fatigue to disability among individuals with TBI who reported clinically significant fatigue. Therefore, participants were included in this subgroup if their mFIS total scores were greater than 38 ($n=24$). Results of the two consecutive multiple linear regressions are presented in Table 4.

In this subgroup, fatigue, injury severity, executive functions, and depression status together explained 64% of the variance in disability among adults with TBI ($F_{4,19}=8.40$, $P<.001$). Of this 64%, fatigue alone accounted for 27% of the variance in disability ($F_{1,19}\Delta=14.17$, $P=.001$). Fatigue ($\beta=.56$) was again the strongest predictor of disability relative to the other covariates in the model ($\beta=.23-.34$). The variance inflation factor for this model ranged from 1.15 to 1.38 and the tolerance ranged from .73 to .87, indicating no collinearity among predictors.

Discussion

The purpose of this study was to examine the unique contribution of fatigue to disability after controlling for injury severity, executive functions, and depression status in a sample of community dwelling adults with a history of TBI. As anticipated, disability was significantly associated with fatigue, injury severity, executive functions, and depression status in this population. Overall, fatigue was found to be not only a significant independent predictor of disability after controlling for these other factors, but also the strongest predictor of disability among these other factors.

The relationship between fatigue and executive functions, particularly in relation to impact on disability, is of particular importance. Consistent with previous findings,(16, 39, 40) increased fatigue in this sample was associated with increased impairment in executive functions. As has been previously shown, impairments in executive functions can result in poorer problem solving and coping skills, leading to increased stress and fatigue and contributing to an ongoing cycle that increases disability.(26, 39) The current study further defines this issue, as the contribution of executive functions to disability appears to decrease when accounting for fatigue, both in the entire sample and in the subgroup of individuals experiencing significant fatigue. Overall, these findings emphasize the need to recognize and address fatigue in individuals with chronic TBI. As there are currently no evidence-based interventions for post-TBI fatigue, further investigation into effective treatments is of critical importance. Finally, these findings suggest that addressing fatigue first, prior to addressing impairments in executive functions, may have a significant impact on minimizing disability.

The relationship between fatigue and executive functions is further complicated by depression. Impairments in executive functions can result in poor adaptive psychological functioning, which, when combined with increased fatigue, can lead to increased depression over time, contributing further to disability.(24, 39) In this sample, depression status was

strongly associated with disability, fatigue, and executive functions. However, depression failed to achieve statistical significance as an independent predictor of disability with the addition of fatigue as a predictor. This seems to indicate that the symptom of depression that contributes the most to disability is fatigue, though further investigation is warranted to confirm this suggestion.

Finally, results of this study found that injury severity at the time of initial injury was not significantly associated with fatigue, executive functions, or depression status, though it was significantly associated with and predictive of disability. The contribution of initial injury severity is particularly notable given that this sample was comprised of individuals with chronic TBI who were independent enough to be living in the community and who reported overall average to above average functioning (low disability). While the results of these analyses cannot explain what contribution initial injury severity makes to disability, it is clear this is a factor that must be considered when exploring disability after TBI, even in a chronic population.

These findings clearly described the importance of fatigue when considering disability after TBI. Further research is required to more fully explore the complex nature of the relationships among fatigue, executive functions, depression, and disability in order to develop the optimal intervention strategies to improve functional and emotional outcomes for individuals with TBI. The unique contribution of fatigue to disability, even after controlling for these other factors, strongly suggests the need to develop additional interventions – whether behavioral, psychological, or pharmacological – targeted specifically at addressing chronic fatigue after TBI.

Study Limitations

This study was a secondary analysis of existing data from an ongoing parent study. All participants were recruited from a convenience sample and lived within a single geographical region. This sample was predominantly made up of Caucasian males. Although the gender distribution is consistent with the broader TBI population, further exploration of the relationships between fatigue and disability by race and gender should be conducted. Additionally, this study relied largely on self-report measures, including measures of both fatigue and disability. Participants experiencing more symptoms (i.e. more fatigue) may be more likely to report greater limitations than those not experiencing these symptoms. Future exploration of this relationship using a performance-based or proxy measure of disability may help to clarify the influence of self-report in the relationship between fatigue and disability.

Additionally, compared to a normative sample of adults with TBI, this sample reported average disability, trending towards above average functioning. While this sample reported levels of disability greater than the general population, it should be noted that this group represents a specific subset of the TBI population, as those with more severe disability are not represented. It is possible that fatigue may play a different role in disability among individuals with more severe disability.

This was a unique population consisting of community dwelling adults with TBI, representing a broad range of time since injury and including those who were currently receiving rehabilitation services, who had received rehabilitation services in the remote past, and who had never received rehabilitation services. While the heterogeneity of the sample reduces statistical power, it increases the ability to generalize to a broader and more representative TBI population.

Conclusions

Fatigue uniquely contributes to disability in a population of community dwelling adults with traumatic brain injury, after controlling for injury severity, executive functions, and depression status. These findings highlight the importance of considering fatigue as it relates to disability in a TBI population. Future research should investigate evidence based interventions to address fatigue among community-dwelling adults with TBI.

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List of Abbreviations

TBI	traumatic brain injury
GCS	Glasgow Coma Scale
MPAI	Mayo Portland Adaptability Inventory
mFIS	Modified Fatigue Impact Scale
FrSBE	Frontal Systems Behavior Scale
SADI	Self Awareness of Deficits Interview

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Table 1

Descriptive Data

	(n=50)	(n=24)*
	Mean (±SD)	Mean (±SD)
Age (years)	47.68 (±15.6)	50.50 (±13.9)
Time Since Injury (months)	58.50 (14–105) [†]	61.50 (12.5–205) [†]
Education (years)	14.62 (±2.7)	14.38 (±2.6)
Disability - MPAI (total standard score) [‡]	44.02 (±13.7)	51.38 (±7.2)
Fatigue – mFIS (total) [‡]	36.06 (±20.7)	54.13 (±10.3)
Executive Function – FrSBE (total T score) [‡]	64.28 (±21.8)	75.54 (±22.7)
Self Awareness - SADI (total) [‡]	1.66 (±2.7)	1.13 (±1.7)
	n (%)	n (%)
Gender (male)	40 (80%)	18 (75%)
Race (white)	48 (96%)	23 (96%)
Married (yes)	22 (44%)	11 (46%)
Ability to drive (yes)	36 (72%)	19 (79%)
Vocational Status		
Full-time	13 (26%)	3 (12%)
Part-time	7 (14%)	6 (25%)
Retired	5 (10%)	1 (4%)
Unemployed	8 (16%)	4 (17%)
Disability	17 (34%)	10 (42%)
Injury Severity [§]		
Uncomplicated Mild	3 (6%)	1 (4%)
Complicated Mild	16 (32%)	9 (38%)
Moderate	6 (12%)	2 (8%)
Severe	25 (50%)	12 (50%)
History of Inpatient Rehabilitation (yes)	37 (74%)	18 (75%)
Depression status (yes) ^{//}	35 (70%)	22 (92%)

* Subgroup: Participants with significant fatigue (mFIS>38)

[†] Median and interquartile range

[‡] Higher scores indicate poorer outcomes

[§] Based on GCS score at time of injury (13–15, neuroradiologic evidence unavailable=uncomplicated mild; 13–5 with positive neuroradiologic findings=complicated mild; 9–12=moderate; 8=severe)

^{//} Indicates current major or minor depression/history of major depression

Table 2

Pearson Correlations (n=50)

	Fatigue	Executive Function	Injury Severity	Depression Status
Disability (MPAI Total Standard score)	$.679^{\dagger}$	$.599^{\dagger}$	$.263^*$	$.511^{\dagger}$
Fatigue (mFIS Total)		$.567^{\dagger}$	$-.025$	$.559^{\dagger}$
Executive Function (FrSBe Total T-score)			$.028$	$.427^*$
Injury Severity (GCS)				$.123$

*
p<.05 †
p<.001; 1-tailed correlations

Table 3**Multiple Linear Regression Analyses (n=50)**

	Disability: Model 1			Disability: Model 2	
	β	P		β	P
Intercept	-	.015	Intercept	-	.010
Executive Function	.47	<0.001	Executive Function	.28	.017
Injury Severity	.22	.050	Injury Severity	.26	.010
Depression Y/N (N ref.)	.28	.021	Depression Y/N (N ref.)	.09	.419
			Fatigue	.47	.001
	$R^2=.48$	<0.001		$R^2=.61$	<0.001
	$R^2_{Adj}=.45$			$R^2_{Adj}=.57$	
				$R^2\Delta=.12$	0.001

Note. $R^2 \Delta$ (F1,45 $\Delta=13.97$, $P=0.001$)

Table 4

Subgroup Analysis: Multiple Linear Regressions (n=24)

	Disability: Model 1		Disability: Model 2	
	β	P	β	P
Intercept	-	<0.001	-	.048
Executive Function	.35	.102	.23	.167
Injury Severity	.20	.283	.34	.033
Depression Y/N (N ref.)	.32	.139	.26	.129
			.56	.001
	$R^2=.37$	.024	$R^2=.64$	.001
	$R^2_{Adj}=.28$		$R^2_{Adj}=.56$	
			$R^2\Delta=.27$	.001

Note. $R^2 \Delta$ (F1,19 Δ =14.17, P =.001)