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Preinjury Health Status of Adults With Traumatic Brain Injury: A Preliminary Matched Case-Control Study

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Objective: To discern whether there is evidence that individuals who sustained a traumatic brain injury (TBI) had the greater odds of preexisting health conditions and/or poorer health behaviors than matched controls without TBI. **Setting:** Brain Injury Inpatient Rehabilitation Unit at Mount Sinai Hospital. Midlife in the United States (MIDUS) control data were collected via random-digit-dialing phone survey. **Participants:** TBI cases were enrolled in the TBI Health Study and met at least 1 of the following 4 injury severity criteria: abnormal computed tomography scan; Glasgow Coma Scale score between 3 and 12; loss of consciousness greater than 30 minutes; or post-TBI amnesia longer than 24 hours. Sixty-two TBI cases and 171 matched MIDUS controls were included in the analyses; controls were excluded if they reported having a history of head injury. **Design:** Matched case-control study. **Main Measures:** Self-reported measures of depression symptoms, chronic pain, health status, alcohol use, smoking status, abuse of controlled substances, physical activity, physical health composite score, and behavioral health composite score. **Results:** Pre–index injury depression was nearly 4 times higher in TBI cases than in matched controls (OR= 3.98, 95% CI, 1.71-9.27; $P = .001$). We found no significant differences in the odds of self-reporting 3 or more medical health conditions in year prior to index injury (OR = 1.52; 95% CI, 0.82-2.81; $P = .183$) or reporting more risky health behaviors (OR = 1.48; 95% CI; 0.75-2.91; $P = .254$]) in individuals with TBI than in controls. **Conclusion:** These preliminary findings suggest that the odds of depression in the year prior to index injury far exceed those reported in matched controls. Further study in larger samples is required to better understand the relative odds of prior health problems in those who sustain a TBI, with a goal of elucidating the implications of preinjury health on post-TBI disease burden. **Key words:** *adult*, *brain injuries*, *data analysis*, *neuropsychology*, *preinjury*, *rehabilitation*, *TBI*, *traumatic*

TRAUMATIC BRAIN INJURY (TBI) is a major public health concern, with an estimated 5.3 million Americans living with TBI-related disabilities. TBI stems from a plethora of causes with varying levels of severity; most common causes include falling, being struck by an object, sports, and military-related injuries.[1] Knowledge of TBI risk factors remains limited, and heterogeneity exists among adults who sustain a TBI concerning clinical representation and post-TBI disease progression.[2,3]

TBI can result in neurologic and physical impairments that can be long-standing and drastically limit activities of daily living.[3,4] Over time, cognitive impairments can manifest in behavioral and mood changes and even long-term neurodegenerative diseases such as Alzheimer and Parkinson diseases.[5,6] Besides debilitating cognitive impairments, severe TBI cases can result in long-term physical disabilities including, but are not limited to, posttraumatic stress disorder, substance abuse, depression, hypertension, visual problems, and general decline in physical motility.[7] The prevalence of prolonged cognitive and multisystem physical health problems post-TBI has contributed to a shift in the field's conceptualization of TBI from an injury event to a disease process. Leaders in the field have begun

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to think about TBI as an evolving condition that may be disease causative and/or disease accelerative.[8] Much of the research supporting the conceptualization of TBI as a chronic disease comes from cohort studies without comparison groups, and the presence of preinjury health problems is seldom considered. As such, it remains unknown whether or to what extent the elevated rates of cognitive and physical health problems described in TBI survivors may be reflective of preexisting disease processes.[3,7]

Determining whether individuals who sustain a TBI have poorer health preinjury than their uninjured counterparts is foundational to quantifying whether and how TBI may exacerbate preexisting health problems or initiate new ones. Certain prior health conditions may predispose an individual to be at a greater risk for a TBI. For example, poor physical health and clinical frailty may lead to falls and have been associated with an increased risk for TBI.[9,10] In addition, certain behavioral risk factors such as illicit drug use and excessive alcohol consumption are associated with higher rates of accidents and falls, which may increase the likelihood of sustaining a TBI.[11,12] The ability to identify modifiable preinjury risk factors for sustaining a TBI could drastically reduce the substantial societal and public health burden attributed to TBIs. Furthermore, the same preinjury conditions that increase TBI risk may interact with injury-related pathology to influence post-TBI course by accelerating cognitive and physical decline.

In this preliminary study, we attempt to better understand whether individuals sustaining a TBI have certain health risk factors in the year prior to index injury that may increase their odds for sustaining a TBI. This understanding will help inform upon whether post-TBI health and disease progression are related to a preexisting disease process or whether TBI initiates a cascade of events leading to poor long-term health consequences. We conducted a demographically matched historical case-control study (1:3 matching ratio) using existing data from a national health survey and harmonized exposure question data with our TBI cohort to test the hypothesis that adults who sustain a TBI have poorer health status and riskier health behaviors in the year *prior to* injury than their uninjured counterparts.

METHODS

Samples

Individuals with TBI

We recruited 87 individuals with TBI via the TBI Health Study conducted at the Brain Injury Inpatient Rehabilitation Unit at Mount Sinai Hospital from 2012 to 2017. To be eligible for the TBI Health Study, individuals with TBI must meet one of the following 4 criteria: an abnormal computed tomographic (CT) scan consistent with TBI pathology; postresuscitation Glasgow Coma Scale (GCS) score between 3 and 12; loss of consciousness (LOC) of more than 30 minutes; or post-TBI amnesia longer than 24 hours.[13] Inclusion criteria are intended to create a study sample of individuals who sustained a complicated mild, moderate, or severe TBI; mild TBI cases did not meet study inclusion criteria.

All participants who enrolled in the TBI Health Study were older than 40 years at the time of injury and consented to study participation. We collected data via in-person and phone interviews with the individual who sustained the TBI. In cases where the patient with TBI was unable to complete a subset of questions, we collected information from a close family member familiar with the patient's medical history. In the TBI sample, we assessed TBI exposure, mechanisms, and severity via the Brain Injury Screening Questionnaire (BISQ). The BISQ is a 20-item questionnaire that uses contextual and etiological cues to facilitate recall of injuries to the head, presence and duration of LOC, and mental status (feelings of being "dazed and confused").[14] Because of missing data for key exposure information, the sample was reduced to 64 individuals with TBI before applying the matching protocol. A majority of individuals with TBI showed an abnormal CT scan positive for TBI pathology (87.1%). Four cases had normal CT scans but scored between 3 and 12 on the GCS, indicating a moderate to severe TBI.[15] In total, 48.8% of cases were classified as complicated mild TBI cases by having abnormal CT scans with TBI pathology but only mild/no concussive symptoms and no posttraumatic amnesia.[16]

Non-TBI controls

We extracted non-TBI controls from the Midlife in the United States (MIDUS) II and MIDUS Refresher cohorts, which are longitudinal, random-digit-dialing follow-up studies of the original MIDUS study of cognitive aging in midlife. The initial MIDUS cohort included noninstitutionalized, English-speaking adults aged 24 to 74 years residing in the contiguous United States ($n = 7108$), and data were from 1995 to 1996.[17] The MIDUS II study was initiated in 2004 to reassess baseline questionnaires and conduct cognitive assessments on the original cohort, now aged 35 to 86 years ($n = 4963$).[18] The MIDUS Refresher study recruited new participants ($n = 3577$) from 2011 to 2014, with an emphasis on a younger and more racially diverse sample, who completed similar assessments and questionnaires to MIDUS II. The average response rate (adjusted for individuals who died) was 86%, thus compiling a comprehensive and representative cohort of adults throughout the United States. Metropolitan populations were oversampled to increase racial, ethnic, and geographic representativeness.[18]

For this study, we identified matched non-TBI controls from both MIDUS II and MIDUS Refresher cohorts. If the MIDUS participant reported "Yes" to having a "history of serious head injury," they were excluded as controls ($n = 306$). Each TBI case was matched with up to 3 control participants on the basis of the following demographic variables: age (caliper width ± 5 years), sex, education, employment, and race.[19]

Past year/preinjury health measures

During data collection, we utilized questions from the MIDUS questionnaire about participant health status and lifestyle in the year prior and at the time of admission. The statement "... *prior to injury*" was added by Mount Sinai researchers to the Health Questionnaires for the TBI Health Study to assess health prior to the index TBI.[13] Because both the TBI Health Study and the MIDUS studies used identical structured interview questions, we harmonized all item-level exposure data to allow direct comparisons between the TBI population and controls by ensuring all demographic and past year health measures coding aligned. Figure 1 illustrates study timeline and exposure/outcome assessment schedule for both cases and controls.

Physical health composite score

In both the TBI Health Study and the MIDUS study, participants endorsed either 1 = yes or 0 = no for "being treated for any of the following [30 conditions] in the year prior [to injury]." We generated a single-item, physical health composite score by summing individual health condition responses.[17,18,20] Physical health composite score was assessed as dichotomous variables, endorsing "3 or more" medical health conditions or "less than 3" conditions.[21]

Behavioral health risk factors

We queried following 4 behavioral health risk factors in the prior year, each coded as binary variables (Yes/No): alcohol use, cigarette smoking, physical inactivity, and substance use, defining each by an affirmative response to the following items. We defined the "alcohol use" as "having alcohol-related problems during the past 12 months."[22] The "smoking status" variable was defined by "smoking cigarettes regularly during the past 12 months." We defined the "substance use" as "any use of drugs or medications without a doctor's prescriptions, in larger amounts than prescribed, or for a longer period during the past 12 months." Examples of substances in the MIDUS questionnaire included the following: sleeping pills, amphetamines, marijuana, hallucinogens, and heroin.[17,18] Consistent with prior work, a "physically active" individual was defined as "engaging in vigorous and/or moderate physical activity several times a week at a paid job, while performing chores in and around home, and/or during leisure or free time."[23,24] The "physical inactivity" variable was reverse scored such that 0 = indicated *no* physical *inactivity* and 1 = indicated physical *inactivity*.

We created a behavioral risk factor composite score consisting of all 4 of these health behaviors: "alcohol use," "smoking status," "substance use," and "physical

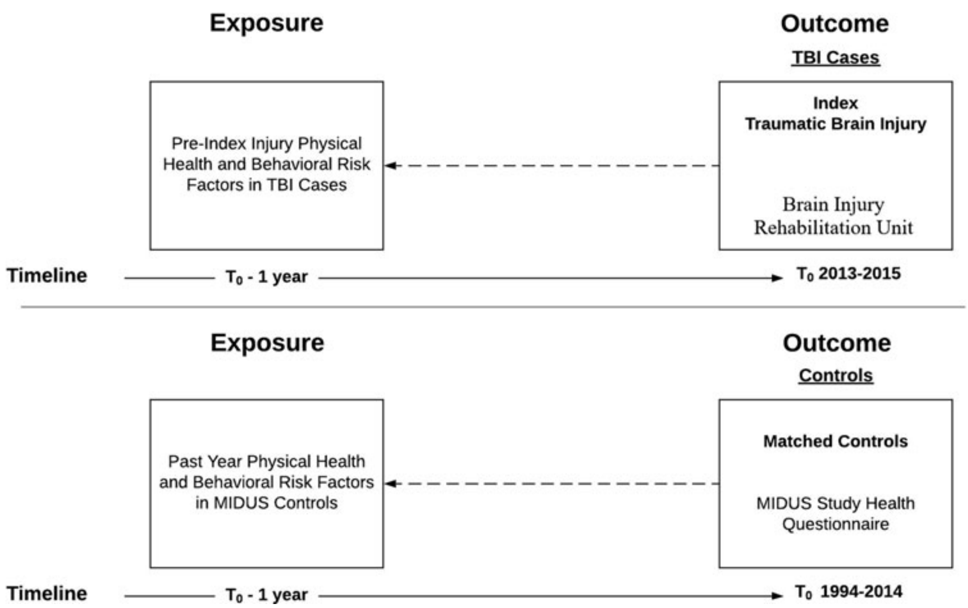

Figure 1. Study timeline of risk factor and outcome assessment of individuals with TBI compared with matched controls in year prior to index date. TBI indicates traumatic brain injury; MIDUS, Midlife in the United States.

inactivity." The composite score ranged from 0 to 4, with 0 indicating no risky health behaviors and 4 indicating endorsement of all 4 risky health behaviors.[24] The behavioral health composite score was assessed as a dichotomous variable: endorsing at least one of the aforementioned risky health behaviors, or endorsing none. The utilization of the behavioral health composite score avoided multiple analyses and splitting *P* values among risky health behaviors.

Additional past 12 months' health measures

We assessed "self-reported physical health" in the year prior to injury on a 5-point Likert scale ranging from poor to excellent. Responses were assessed on an ordinal level and then recategorized as a binary variable, "excellent/very good/good" and "fair/poor." In addition, we queried "self-reported chronic pain" during the past 12 months as a binary (Yes/No) exposure defined as "pain that persisted beyond the time of normal healing and has lasted anywhere from a few months to many years." Finally, to further assess whether depression alone was a risk factor for TBI, we assessed "self-reported depressive symptoms" as "during the past 12 months, was there ever a time when you felt sad, blue, or depressed for 2 weeks or more in a row." Individuals endorsed having "self-reported depressive symptoms" if they responded "Yes" or "I did not feel depressed because I was on antidepressant medication" for the earlier question.

Study variables

Sociodemographic covariates included age, sex, race (White, African American, other), employment (employed/working for pay or unemployed), and education (less than high school, high school, some college, and college degree). While not included as covariates for matching, Spanish ethnicity, marital status, and TBI severity frequencies were assessed within the study population. Primary predictor variables were all self-reported and included the following: health status, chronic pain, depressive symptoms, excessive alcohol use, smoking status, substance abuse, physical inactivity, physical health composite score, and behavioral health composite score.

Statistical analyses

The specific method of matching used between TBI cases and controls was a "greedy matching," or nearest neighbor matching without replacement. The greedy matching algorithm found the closest control for each TBI case that produced a matching sample with balanced distribution of the demographic covariates across the 2 groups.[19] We performed descriptive analyses on all demographic and outcome variables to assess variable distribution and to describe both cases and controls. To assess the balance of variables after matching, standardized differences were reported, and the variables with differences greater than 10% were considered for further adjustment in the model.[25,26]

We performed conditional logistic regression analyses for primary and secondary exposures and reported odds ratio (OR) with 95% CI. We compared the frequencies of prior year exposure to behavioral and physical health risk factors in cases (ie, those with TBI) and controls to determine the relationship between these exposures and TBI case status.[27] ORs were estimated to assess the odds of prior year physical health and behavioral exposure in TBI cases compared with matched controls.[28] Models were conditional on the matched strata. We conducted subgroup analyses by age and sex to examine whether the association differed among prespecified subgroups. Subgroup analyses by age were stratified as 65 years or more and less than 65 years at the time of interview.[4] We considered a *P* value of less than .05 to be statistically significant for both physical and behavioral health risk factor domains.[29]

All statistical analyses were performed using SAS enterprise guide SAS Enterprise Guide (version 7.1; SAS Institute Inc, Cary, North Carolina) and SAS 9.4.

RESULTS

We matched 62 patients with TBI with controls in a 1:3 ratio (96.9% matching rate). The final cohort included 62 individuals with TBI and 171 matched MIDUS controls (see Figure 2).

Table 1 presents the overall demographic characteristics of the TBI cases and non-TBI controls after matching. The standardized difference in age was greater than 10% (0.18 for mean and 0.16 for median). The standardized differences postmatching for sex, race, employment, and education were all less than 10%.[26]

Table 1 shows the proportions and balance of the self-reported past year health and behavioral outcomes in the TBI and non-TBI samples after matching. A majority of cases (80.7%) and controls (84.1%) reported their previous years' health status as good to excellent. A smaller proportion of those with TBI reported chronic pain in the year prior (17.7%) than those without a TBI (33.3%). A higher proportion of individuals with TBI reported depressive symptoms in the year prior than the controls (27.4% vs 9.9%). There were higher proportions of individuals reporting excessive alcohol use, current smoking status, and substance abuse in the TBI sample, as seen in Table 1.

To illustrate results of the primary analyses, Table 2 shows the results of the conditional logistic regression while accounting for matched pairs. We found the odds of having prior year depressive symptoms were roughly

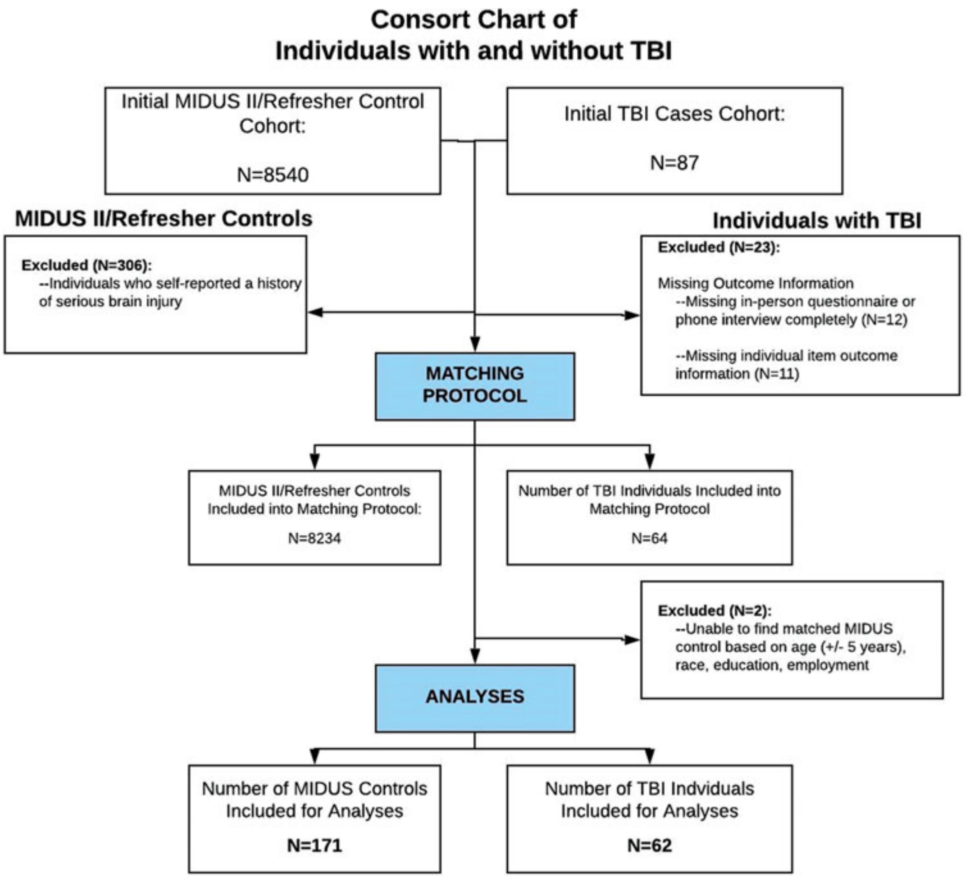

Figure 2. Consort chart of individuals with and without TBIs used for matching protocol and final analyses. For analyses, n = 62 cases and n = 171 controls were retained. TBI indicates traumatic brain injury; MIDUS, Midlife in the United States. This figure is available in color online (www.headtraumarehab.com).

TABLE 1 *Demographic characteristics and self-report exposures of matched individuals with and without TBI at baseline (N = 233)*

Participants' demographic characteristics and self-reported exposures	Total (n = 233)	TBI (n = 62)	No TBI (n = 171)	Standardized differences (absolute value)
Age[a]				
Mean ± SD	65.62 ± 12.17	66.53 ± 12.81	65.30 ± 11.95	0.18[b]
Median (IQR)	68 (58-75)	69 (59-75)	68 (58-74)	0.16[b]
Sex[a]				
Male	160 (68.7%)	42 (67.7%)	118 (69.0%)	0.03
Female	73 (31.3%)	20 (32.3%)	53 (31.0%)	0.03
Race[a]				
White	177 (76.0%)	47 (75.8%)	130 (76.0%)	0.01
African American	23 (9.9%)	6 (9.7%)	17 (9.9%)	0.01
Other	33 (14.2%)	9 (14.5%)	24 (14.0%)	0.01
Employment[a]				
Employed	120 (51.5%)	30 (48.4%)	90 (52.6%)	0.08
Unemployed	113 (48.5%)	32 (51.6%)	81 (47.4%)	0.08
Education[a]				
<High school	23 (9.9%)	6 (9.7%)	17 (9.9%)	0.01
High school	35 (15.0%)	9 (14.5%)	26 (15.2%)	0.02
Some college	26 (11.2%)	7 (11.3%)	19 (11.1%)	0.01
College degree	149 (63.9%)	40 (64.5%)	109 (63.7%)	0.02

(*continues*)

TABLE 1 *Demographic characteristics and self-report exposures of matched individuals with and without TBI at baseline (N = 233)* (Continued)

Participants' demographic characteristics and self-reported exposures	Total (*n* = 233)	TBI (*n* = 62)	No TBI (*n* = 171)	Standardized differences (absolute value)
Marital status				
Married	148 (63.5%)	36 (58.1%)	112 (65.5%)	0.15
Separated	5 (2.1%)	2 (3.2%)	3 (1.8%)	0.09
Divorced	22 (9.4%)	2 (3.2%)	20 (11.7%)	0.33
Widowed	31 (13.3%)	9 (21.0%)	22 (12.9%)	0.05
Never married	26 (11.2%)	13 (21.0%)	13 (7.6%)	0.39
Missing	1 (0.4%)	2 (3.2%)	1 (0.6%)	0.11
Spanish ethnicity				
Yes	19 (8.2%)	10 (16.1%)	9 (5.3%)	0.36
No	212 (91.0%)	50 (80.6%)	162 (94.7%)	0.44
Missing	2 (0.9%)	2 (3.2%)	0 (0.00%)	0.26
TBI severity				
Mild/complicated mild		30 (48.4%)		
Moderate/severe		32 (51.6%)		
LOC ≤30 min		10 (16.1%)		
LOC >30 min		15 (24.2%)		
PTA ≥24 h		22 (35.5%)		
Health status				
Fair/poor	38 (16.3%)	11 (17.7%)	207 (15.7%)	0.11
Excellent/very good	194 (83.3%)	50 (80.7%)	144 (84.1%)	0.28
Missing	1 (0.4%)	1 (1.6%)	0 (0.00%)	0.18
Chronic pain				
Yes	68 (29.2%)	11 (17.7%)	57 (33.3%)	0.36
No	164 (70.4%)	50 (80.6%)	114 (66.7%)	0.32
Missing	1 (0.4%)	1 (1.6%)	0 (0.00%)	0.18
Depressive symptoms				
Yes	34 (14.6%)	17 (27.4%)	17 (9.9%)	0.46
No	198 (85.0%)	44 (71.0%)	154 (90.1%)	0.50
Missing	1 (0.4%)	1 (1.6%)	0 (0.00%)	0.18
Physical health composite				
<3 conditions	129 (55.4%)	29 (46.7%)	100 (58.5%)	0.24
≥3 conditions	104 (44.6%)	42 (53.3%)	71 (41.5%)	0.24
Behavioral health composite				
0	85 (36.5%)	19 (30.6%)	66 (38.6%)	0.17
≥1	148 (63.5%)	43 (69.4%)	105 (61.4%)	0.01
Excessive alcohol use				
Yes	17 (7.3%)	7 (11.3%)	10 (5.9%)	0.19
No	216 (92.7%)	55 (88.7%)	161 (94.2%)	0.20
Currently smoking				
Yes	19 (8.2%)	7 (11.3%)	12 (7.0%)	0.15
No	214 (91.8%)	55 (88.7%)	159 (93.0%)	0.15
Substance abuse				
Yes	24 (10.3%)	9 (14.5%)	15 (8.8%)	0.21
No	209 (89.7%)	53 (85.5%)	156 (91.2%)	0.18
Physical inactivity				
Yes	123 (52.8%)	33 (53.3%)	90 (52.6%)	0.01
No	110 (47.2%)	29 (46.8%)	81 (47.4%)	0.01

Abbreviations: LOC, loss of consciousness; PTA, posttraumatic amnesia; TBI, traumatic brain injury.
[a]Demographic variables used in nearest neighbor matching protocol.
[b]Standardized differences greater than 10%, adjusted for residual confounding in final models. From Marquez de la Plata et al.[2]

4 times higher in TBI cases than in matched controls (OR = 4.16; 95% CI, 1.79-9.67; $P = .001$). The odds of having the remaining health and behavioral health risk factors in the past year did not significantly differ between TBI cases and controls, though it should be noted that several ORs (eg, past year alcohol use, smoking, and abuse of illegal substances) suggested the greater odds in the TBI group.

TABLE 2 *Odds ratios of past year exposures in individuals with TBI and non-TBI controls*

Participant prior year self-reported exposures[a]	Matched sets ($n = 62$), OR (95% CI)	*P*
Self-reported depression	4.16 (1.79-9.67)	.001[b]
Self-reported chronic pain	0.56 (0.27-1.14)	.11
Self-reported poor health status	1.36 (0.57-3.24)	.49
Physical health composite score ≥ 3 conditions	1.61 (0.86-3.01)	.14
Behavioral health composite score >0 risk factors	1.52 (0.77-3.00)	.23
Excessive alcohol use	2.05 (0.74-5.71)	.17
Currently smoking	1.93 (0.67-5.55)	.22
Reported abuse of illegal/controlled substance	2.22 (0.88-5.59)	.09
Self-reported physical inactivity	0.95 (0.49-1.73)	.81

Abbreviation: TBI, traumatic brain injury.
[a]All exposures represent separate analyses.
[b]Significant with *P* value less than .05.

The results of subgroup analyses for each analytic outcome, stratified by sex and age (≥65 or <65 years), are reported in Table 3. The odds of having prior year pre–index injury depressive symptoms were significantly higher in *male* TBI cases than in male controls (OR = 7.31; 95% CI, 2.39-22.30; $P \leq .001$) but not in females (OR = 1.62; 95% CI, 0.42-6.27; $P = .459$). Remaining differences in preinjury health status by sex did not reach statistical significance, but nonetheless warrant mention in this preliminary study. When stratified by age, the odds of having prior year pre–index injury exposure of depressive symptoms were 7.32 times higher in TBI cases 65 years or older than in controls 65 years or older (OR = 7.32; 95% CI, 2.02-26.52; $P = .003$), but the odds were not significantly different in those younger than 65 years (OR = 2.38; 95% CI, 0.74-7.72; $P = 0.148$). The odds of reporting prior year excessive alcohol use were 6.58 times higher in TBI cases 65 years or older than individuals 65 years or older without TBI (OR = 6.58; 95% CI, 1.17-37.1; $P = .033$ vs OR = 0.82; 95% CI; 0.17-3.97; $P = 0.808$ in the younger subgroup). Finally, the odds of smoking regularly in the year prior to injury was 4.29 times higher in TBI cases 65 years or older than in controls 65 years or older (OR = 4.29; 95% CI, 1.03-17.98; $P = .0462$). No remaining subgroup analyses of the behavioral health risk factors yielded significant differences between TBI cases and controls.

TABLE 3 *Odds ratios of past year exposures in individuals with traumatic brain injury and controls stratified by age (≥65 years vs <65 years) and sex*

Participant prior year exposures[a] by age and sex	Matched sets ($n = 62$), OR (95% CI)	*P*
Self-reported depressive symptoms		
≥65 y old	7.32 (2.02-26.5)	.002[b]
<65 y old	2.38 (0.74-7.72)	.15
Male	7.31 (2.39-22.3)	.0005[b]
Female	1.62 (0.42-6.27)	.49
Self-reported chronic pain		
≥65 y old	0.49 (0.20-1.22)	.12
<65 y old	0.77 (0.24-2.45)	.65
Male	0.63 (0.20-2.03)	.44
Female	0.52 (0.21-1.30)	.16
Self-reported poor health status		
≥65 y old	1.28 (0.44-3.74)	.65
<65 y old	1.97 (0.41-9.45)	.40
Male	0.61 (0.07-5.72)	.67
Female	1.57 (0.61-4.02)	.35
Physical health composite score ≥ 3 conditions		
≥65 y old	1.30 (0.60-2.85)	.51
<65 y old	2.23 (0.79-6.30)	.13
Male	1.44 (0.43-4.85)	.56
Female	1.96 (0.88-4.35)	.09
Behavioral health composite score >0 risk factors		
≥65 y old	1.49 (0.61-3.63)	.38
<65 y old	1.55 (0.54-4.45)	.42
Male	0.74 (0.22-2.48)	.62
Female	2.07 (0.88-4.87)	.10
Excessive alcohol use		
≥65 y old	6.58 (1.17-37.1)	.03[b]
<65 y old	0.82 (0.17-3.97)	.81
Male	7.94 (0.77-81.8)	.08
Female	1.34 (0.39-4.60)	.64
Currently smoking		
≥65 y old	4.29 (1.03-18.0)	.05[b]
<65 y old	0.44 (0.05-3.88)	.46
Male	0.68 (0.10-4.51)	.69
Female	3.39 (0.92-12.5)	.07
Reported abuse of illegal/controlled substance		
≥65 y old	3.62 (0.94-14.0)	.06
<65 y old	1.64 (0.44-6.12)	.46
Male	4.55 (0.67-31.1)	.12
Female	1.71 (0.58-5.04)	.33
Self-reported physical inactivity		
≥65 y old	0.96 (0.43-2.19)	.93
<65 y old	0.90 (0.34-2.39)	.83
Male	0.42 (0.12-1.36)	.15
Female	1.28 (0.59-2.77)	.54

[a]All exposures represent unique analyses.
[b]Significant with *P* value less than .05.

DISCUSSION

The current preliminary study complements the accumulating evidence of elevated post-TBI disease burden by investigating whether and what types of health conditions were already higher before the injury among those who sustain a TBI than in their uninjured counterparts. Our largely null findings suggest that, with the notable exception of past year depression, adults who sustain a TBI do not differ markedly in past year health compared with individuals who do not sustain a TBI. When considered in context of existing literature reporting high post-TBI disease burden, the current findings may suggest that many post-TBI health conditions do not simply reflect premorbid differences.

However, the current findings should be considered in the context of the study's small sample. While our preliminary study contributes important information to the conceptualization of post-TBI disease burden, we acknowledge that the limitation of small TBI case sample size leads to a higher likelihood of type 2 error and lack of power to detect the significance of effect size estimates. There is some indication that the odds of prior year alcohol use, smoking, and abuse of illicit substances were also greater in the TBI sample, particularly those older than 65 years; in a larger sample, these differences may have reached statistical significance. The odds of self-reported poor health status and the odds of reporting more than 3 health conditions are somewhat higher in cases, particularly those younger than 65 years. Of potential interest is the trend toward the lower odds of self-reported chronic pain in the TBI group, which is surprising, given that chronic pain is one of the most commonly reported problems among TBI survivors and the prevalence in some subgroups of TBI survivors is nearly double that of their uninjured peers.[30] In any case, the current results and their implications should be interpreted as preliminary. One of our greatest study strengths was the utilization of a well-established TBI case definition based on inpatient rehabilitation severity criterion and the use of incident TBI diagnoses to accurately classify cases and injury timeline.[13] Nonetheless, this strict study inclusion criterion limited our pool of eligible TBI cases since mild TBI cases do not usually receive inpatient rehabilitation services and thus would not be considered for the TBI Health Study.

Concerning our preliminary results, when matched on age, sex, race, education, and employment, the odds of having depressive symptoms in the year prior to injury for cases with TBI were roughly 4 times higher than non-TBI controls. Previous literature has shown that individuals who sustained a TBI have higher rates of depressive symptoms than the general population.[5] Approximately half of all people with TBI report depressive symptoms 1 year post-TBI, which are often attributed to both the neurophysiological changes within the brain and the emotional response to TBI-related disability.[2,31,32] Current findings suggest that a preinjury history of depressive symptoms may contribute to high rates of depression in this group. The odds of preinjury depressive symptoms were particularly high among males and those older than 65 years, consistent with prior research identifying depression as a significant risk factor for late-life TBI.[10] The current findings may also help identify individuals with the increased odds of sustaining a TBI; namely, those with depressive symptoms and/or undergoing treatment of depression (particularly among males and adults older than 65 years), and older adults who engage in excessive alcohol use or cigarette smoking. Previous work has shown that older adults with depression have higher incident and overall frailty as measured by a short performance physical battery.[10,31] The higher rates of frailty in older individuals with depression can lead to an increased risk for injurious falls that could potentially result in a TBI. Current findings of the elevated odds of past year alcohol use among those with TBI who are 65 years or older coincide with previous literature showing that excessive alcohol use is associated with higher rates of injurious falls that may result in more injuries to the head.[12]

There are some additional limitations to this study beyond sample size and low power, which warrant consideration. The TBI Health Study was limited to those who received acute inpatient rehabilitative care for TBI, so findings may not generalize to those who do not seek or require extensive medical treatment. Furthermore, methods for selection into the MIDUS study differed from that of our study; in particular, MIDUS recruitment was not related to an index event. TBI case selection depended on an index TBI event and inpatient care, thus leading to an increased likelihood of capturing prior year exposures in cases relative to controls. In addition, while MIDUS participants who reported a "history of serious head injury" were excluded from the study, we cannot guarantee that all MIDUS controls included in the analyses never experienced a TBI. This nondifferential misclassification makes the direction of bias toward the null. The retrospective study design of both our TBI Health Study and MIDUS study are subject to recall bias in the reporting of prior year health conditions, and post-TBI cognitive impairment may result in underreporting of preinjury health conditions and behaviors and thereby contribute to the null findings between TBI cases and controls.[33] For TBI cases, approximately 35.5% of case responses were provided by a proxy informant and 9.7% used a combination of proxy and self-reporting methods; proxy report may differ in accuracy from self-report.[34] Finally, because we only matched TBI cases to controls on the basis of age, sex, race, employment, and education, there may be unmeasured confounding from covariates on which groups were not matched.

There are several important strengths to the design of this study. By using the same questionnaires in the TBI Health Study as those utilized in the MIDUS Health Questionnaires (adding only the "prior to injury" clause), we were able to readily harmonize data from TBI cases and controls for direct comparison. And as mentioned earlier, our definition of TBI was based on inpatient rehabilitation and their validated TBI severity indices, thus ensuring accurate TBI case classification. Likewise, the use of random population controls instead of hospital or deceased individuals reduced the amount of Berkson's selection bias, or bias from hospital-based control sampling.[35] Demographically matched TBI cases and controls ensured the 2 groups were similar, allowing for a more robust estimate of association of prior year health conditions and sustaining a TBI.

The current findings should be investigated for replicability in a larger study. It is possible that some of the null findings may become significant with a larger sample, which would lend support to the idea that at least some post-TBI behavioral problems are reflective of preinjury health status. In particular, the odds of having certain behavioral health conditions, particularly substance use, are higher in the year prior to injury among those with TBI than in uninjured counterparts but did not reach the threshold for statistical significance in the present study. High rates of substance use prior to TBI have in fact been well documented in the literature.[30,36] In addition, future research in larger samples might consider matching on additional factors such as ethnicity and marital status and also be better suited to investigate the individual components of the health summary and composite scores used herein, which may provide more insight into specific health conditions and their relationship to sustaining a TBI. Certain behavioral health conditions such as physical inactivity were dichotomized to fit the logistic regression model, but assessing these risk factors on multiple levels may yield more granular estimates.

In summary, we found the higher odds of preinjury depressive symptoms among individuals who sustain a TBI than matched, non-TBI controls. Older individuals and males who sustain a TBI have particularly the elevated odds of prior year depressive symptoms. Previous literature documenting elevated disease burden among individuals with TBI has suggested that TBI is disease causative and/or disease accelerative, but it is important to consider whether these observed differences may simply reflect a continuation of elevated preinjury health conditions.[37] Although individuals with TBI in the current study were not significantly more likely to report medical health problems in the past year than controls, observed trends of greater behavioral health problems among those with TBI warrant further study in larger samples with more detailed characterization of other potentially relevant behavioral risk factors such as sleeping habits, diet, sexual health, and health management practices. The current findings may help inform secondary and primary TBI prevention methods to reduce the enormous individual and population-level economic and public health burden of TBI.

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