

Traumatic Brain Injury in a Community-Based Cohort of Homeless and Vulnerably Housed Individuals

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Abstract

We characterized traumatic brain injury (TBI) and studied its associations with mental and physical health in a community cohort of homeless and vulnerably housed individuals. Detailed mental and physical health structured interviews, neuropsychological testing, and multimodal magnetic resonance imaging (MRI) were performed on 283 participants. Two TBI participant groups were defined for primary analyses: those with a self-reported history of TBI and those with MRI confirmation of TBI. By self-report, 174 participants (61.5%) reported a previous serious head or face injury (symptomatic or asymptomatic), with 100 (35.3%) experiencing symptoms consistent with TBI (any post-injury loss of consciousness, confusion, or memory loss). Persons self-reporting TBI had poorer current mental and physical health, more ongoing neurological symptoms, and a higher rate of mood disorders, compared to those with no TBI. The presence of a mood disorder, a TBI history, and an interaction between these factors contributed to lower mental health. There was evidence of TBI in 20 participants (6.9%) on clinical MRI sequences. These participants had globally lower cortical gray matter volumes and lower white matter fractional anisotropy (FA) values. Neurocognitive test scores positively correlated with both FA and cortical gray matter volumes in participants with MRI evidence of trauma. Previous TBI is associated with poorer mental and physical health in homeless and vulnerably housed individuals and interacts with mood disorders to exacerbate poor mental health. Focal traumatic lesions evident on MRI are associated with diffusely lower gray matter volumes and white matter integrity, which predict cognitive functioning.

Keywords: concussion; diffusion tensor imaging; gray matter volume; homeless; traumatic brain injury

Introduction

THE MENTAL AND PHYSICAL HEALTH of homeless and vulnerably housed people is affected by multiple comorbidities and is associated with an age-adjusted mortality rate as high as 8 times that of the general population.¹ Instruments to assess the risk and consequences of comorbidity are evolving. The well-validated Charlson index aggregates 22 deleterious health conditions, assigns individual weights, and produces a score predictive of mortality, quality of life, and care utilization.^{2,3} Traumatic brain injury (TBI), not included in the Charlson index, is a common and important comorbidity among the homeless and vulnerably housed with prevalence estimates as high as 53%.⁴ In the general population, TBI is a major cause of disability and is the leading cause of death among persons in the United States under age 44.⁵ Even mild injuries may alter developmental trajectories and predispose to multiple psychiatric disorders.^{6,7} TBI is of particular interest in the

homeless and vulnerably housed as a possible contributor to poor mental and physical health as well as a potential risk factor for the onset and chronicity of homelessness.

Identifying TBI in the homeless and vulnerably housed remains challenging. Neuroimaging may be particularly informative given that cognitive deficits, common to both homelessness and TBI, may lead to inconsistencies in self-report and challenges for reliable assessment.

Our study aims were to assess TBI and its consequences using detailed historical and neuroimaging assessments in a community-based cohort of homeless and vulnerably housed participants. We obtained comprehensive histories of mental and physical illness, TBI, neuropsychological testing, and multimodal MRI to explore structure-function relationships. Our hypotheses were: 1) TBI would be an independent contributor to poorer mental and physical health; 2) TBI would negatively interact with comorbid illness to produce disproportionately poor health outcomes; and 3) neuroimaging

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evidence of TBI would be high in this cohort and associate with poor cognitive functioning.

Methods

Recruitment

Low-income, single-room occupancy (SRO) housing was the site for recruitment of 308 participants, supplemented by 67 individuals living in the same neighborhood recruited from the downtown community court.⁸ Because of our neuroimaging focus, the present analysis excluded participants with missing or poor-quality magnetic resonance imaging (MRI) scans (Fig. 1).

Measures

Questionnaires. Demographic information, a longitudinal housing history, and a review of legal history were gathered.⁸ Health-related quality of life was assessed with the Short-Form 36-item Health Survey (SF-36).⁹

Traumatic brain injury definition and severity. Participants were asked “Have you ever had a serious head/face injury?” to elicit information about their most severe TBI. The duration of any loss of consciousness (LOC) and confusion or memory loss post-

injury was recorded, as was the cause of injury. This self-report information was used to create two groups: 1) the “No-TBI” group, defined as participants who responded negatively to our question and had no evidence of trauma on MRI, and 2) the “TBI” group, defined as participants who responded affirmatively to our question and endorsed post-injury symptoms of either LOC or confusion/memory loss. Participants reporting a serious head/face injury without post-injury symptoms and without evidence of traumatic damage on MRI were excluded from further analysis. The TBI group was subdivided based on severity, with “mild TBI” defined as self-reported TBI with LOC <30 min and confusion/memory loss <1 day, and “moderate/severe TBI” defined as LOC ≥30 min or confusion/memory loss ≥1 day, according to the World Health Organization classification of TBI severity.¹⁰ Finally, participants with traumatic injury on MRI were coded as the MRI + TBI group, irrespective of self-report.

Physical illness. A structured interview and review of systems was used to record past and current physical illness. The responses were used to calculate the Charlson comorbidity index for each participant, using the original Charlson weighting scheme and adding an additional point for each decade over 40.^{2,3} Serological testing for human immunodeficiency virus (HIV) and hepatitis C virus (HCV) was obtained; samples positive for HCV were submitted for qualitative polymerase chain reaction.

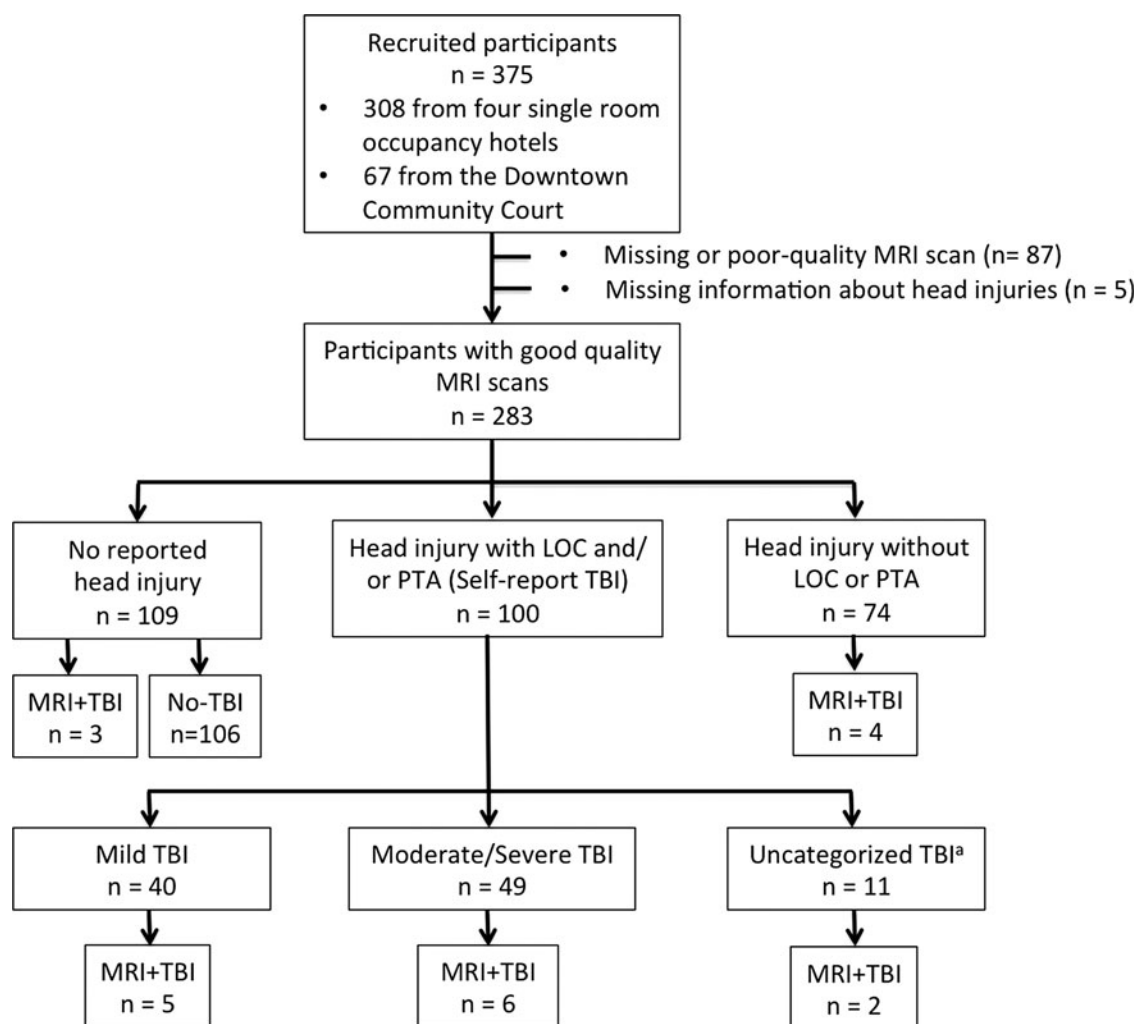


FIG. 1. Flow chart of traumatic brain injury (TBI) categorization based on self-report information and MRI (MRI + TBI). LOC, loss of consciousness; MRI, magnetic resonance imaging; PTA, post-traumatic amnesia.

Mental illness and substance use. The Mini-International Neuropsychiatric Interview was supplemented by a psychiatrist-administered clinical examination in all participants. A urine sample was obtained for drug screening. Where available, a history of hospitalization for mental illness was reviewed from medical records dating back as far as 50 years. All information was used by a research psychiatrist to make diagnoses using the Best Estimate Clinical Evaluation and Diagnosis form, adapted to *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) criteria, with previously reported good reliability.⁸ Suicidal ideation was assessed by self-report using the Beck Depression Inventory (score ≥ 1 on the suicidal ideation item) and the Maudsley Addiction Profile (score ≥ 2 ["sometimes"] on thoughts of ending your life).⁸

Cognition. Tests of premorbid IQ (Wechsler Test of Adult Reading; WTAR),¹¹ response inhibition (Stroop Color-Word Test),¹² immediate memory (Hopkins Verbal Learning Test [HVLT] Revised),¹³ sustained attention (Rapid Visual Information Processing task signal detection score),¹⁴ mental flexibility (Intra-Dimensional Extra-Dimensional test total adjusted errors score),¹⁴ and decision making (Iowa Gambling Task total net score)¹⁵ were administered under the supervision of a neuropsychologist (A.T.). Research assistants rated test score validities based on participants' engagement with and adherence to each task. Scores were considered invalid and excluded from analyses if rated "questionably valid" or lower. Cognitive test scores are presented in t-score units for illustrative purposes; nonetheless, analyses were conducted on the raw scores.

Imaging

Image acquisition. T1-weighted anatomic (1-mm slices), T2-weighted fluid attenuated inversion recovery, susceptibility-weighted imaging, and diffusion brain MRIs were obtained using a Philips 3 Tesla Achieva scanner (Philips, Best, The Netherlands).

For diffusion tensor imaging (DTI) acquisition, each participant was scanned twice and the data averaged. Parameters were as follows: 32 directions; repetition time = 6452 ms; echo time = 60 ms; acquisition matrix = 100×99 ; REC voxel = $2.0 \times 2.0 \times 2.0$; flip angle = 90 degrees; field of view = 224×224 ; 70 contiguous 2.2-mm slices; sensitivity encoding = 1.8; max b-factor = 700; echo planar imaging = 51; and autoshim, acquisition time = 3:45.8 min. A neuroradiologist (T.V.) reviewed all images. Scans with cortical encephalomalacia were reviewed separately by two certified neurologists (one vascular and one specializing in TBI), and, in 6 cases, by a second neuroradiologist (M.H.) for confirmation that the lesions were likely traumatic in etiology. Examples of pathologies interpreted as traumatic in origin appear in Figure 2.

Image processing: volumetric. Cortical lobar white and gray matter volumes were identified using the FMRIB Software Library (FSL) FAST 4.1 tissue segmentation tool¹⁶ and Freesurfer v5.3.¹⁷

Image processing: diffusion tensor imaging. Fractional anisotropy (FA) images were created by fitting a tensor model to the raw diffusion data using FMRIB's Diffusion Toolbox and then brain-extracted using the Brain Extraction Tool.¹⁸

Fractional anisotropy of the corpus callosum. Mean FA of the corpus callosum (CC) was extracted by binarizing the JHU-ICBM-labels-1 mm template from FSL to include only the CC. Each participant's nonlinearly registered FA scan was then masked with the binarized template, and mean FA was computed for each masked image by FSL.

Statistical analysis

Statistical tests were carried out with SPSS software (version 23.0; SPSS, Inc., Chicago, IL) and were two-tailed. Descriptive statistics addressing demographic and clinical differences between

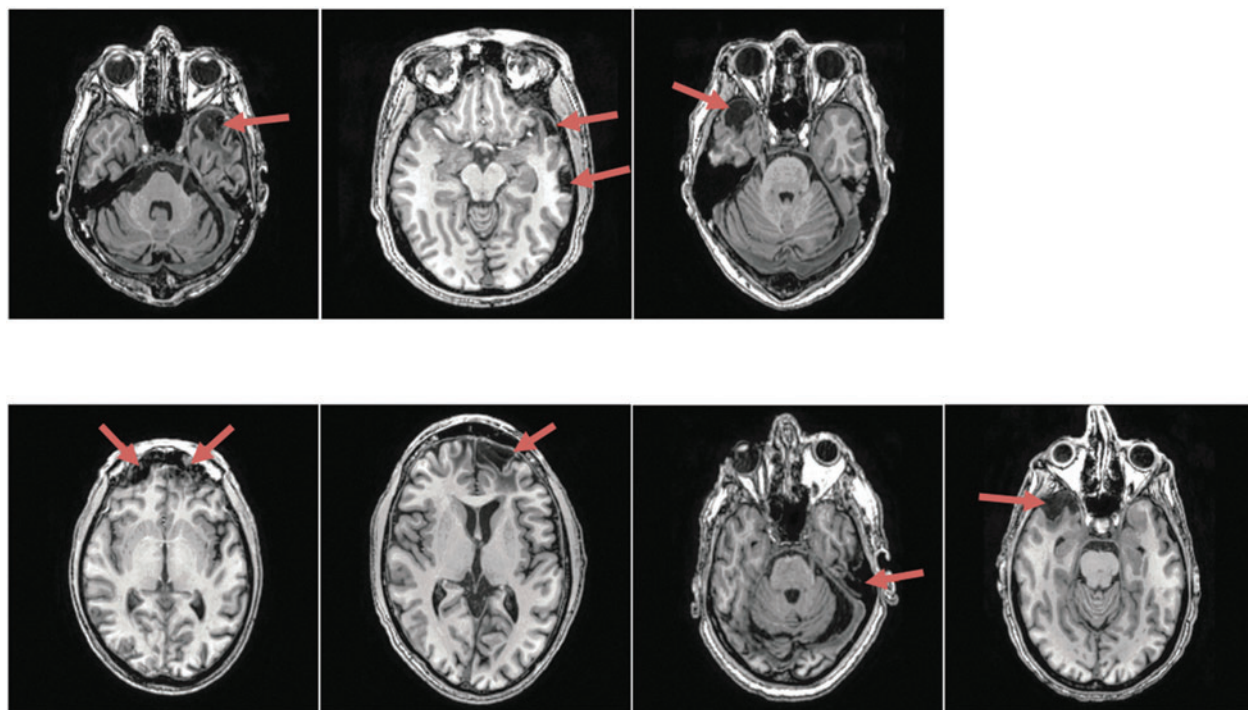


FIG. 2. Representative case examples of traumatic brain injury visible on MRI. Top row: subjects who endorsed *no history* of head or face injury. Bottom row: subjects who endorsed a head or face injury without any loss of consciousness or confusion or memory loss. None of these participants reported a history of stroke. MRI, magnetic resonance imaging; TBI, traumatic brain injury.

groups used *t*-tests, chi-squared tests, and Fisher's exact test, where indicated.

Self-reported traumatic brain injury comparisons. Logistic regression was used to evaluate whether neurological symptoms and mood disorders were associated with self-reported TBI severity. To evaluate the effect of self-reported TBI on cognition, an analysis of covariance (ANCOVA; adjusting for age and years of education) was performed. An additional ANCOVA was used to examine the effect of self-reported TBI and mood disorders on mental and physical health (indexed by SF-36 scores) after adjusting for other multimorbidities using the Charlson comorbidity score.

Imaging and cognitive characteristics of participants with magnetic resonance imaging evidence of trauma (magnetic resonance imaging + traumatic brain injury). To examine differences between the no-TBI and the MRI + TBI group in total cerebral gray matter and in cognition, we used a 2:1 matching strategy, comparing 40 no-TBI participants with 20 MRI + TBI subjects. Participants were matched on variables known to be associated with cognition and brain structure: age; years of education; sex; MRI evidence of stroke; schizophrenia; HCV status; and HIV status. We used *t*-tests to compare cognitive test scores and total cerebral gray matter differences between groups.

To test the hypothesis that localized traumatic lesions on MRI may be associated with global gray matter volume reductions, we eliminated cortical areas with focal injury from the analysis. As an example, to compare the MRI + TBI with no-TBI participants on frontal lobe gray matter volume, we only included MRI + TBI participants with no evidence of damage to the frontal lobes, but who did have damage elsewhere. Thus, *t*-tests were performed that excluded the cerebral lobes showing signs of injury and included only lobes that appeared uninjured on conventional MRI.

For DTI analyses, voxel-wise statistical analysis of the FA data was carried out using Tract-Based Spatial Statistics (TBSS)¹⁹ and Randomise.²⁰ All participants' FA data were projected onto a mean FA tract skeleton followed by voxel-wise cross-participant statistics. The number of permutations was set at 5000, and threshold-free cluster enhancement with correction for family-wise error rate was used. The $p < 0.05$ *t*-contrast maps were projected on the mean FA images.

Finally, Pearson's correlation coefficients were used within the MRI + TBI group to assess associations between cognition and 1) frontal and temporal lobe gray matter volumes and 2) CC FA.

Results

Clinical features of self-reported traumatic brain injury and comorbidity

The demographic and clinical characteristics of included participants are reported in Table 1, with a participant recruitment flow diagram in Figure 1. A serious head or face injury was reported by 174 of 283 (61.5%) of participants, with 100 (35.3%) participants also reporting LOC, confusion, or memory loss post-injury (TBI group). Of the TBI group, 40 were classified as mild, 49 as moderate/severe, and 11 as uncategorized. For a detailed classification according to self-reported LOC and post-traumatic amnesia (PTA), see Supplementary Table 1 (see online supplementary material at <http://www.liebertpub.com>). There were 106 participants without a self-reported serious head/face injury or any evidence of trauma visible on MRI (no-TBI group).

The prevalence of TBI was similar among men and women. Participants with a self-reported history of TBI were significantly older, more likely to have been criminally charged, and more likely

to have a lifetime history of alcohol dependence (Table 1). Rates of other substance dependence diagnoses did not differ, consistent with urine drug screens ($N = 178$). The most common cause of TBI was assault, accounting for 52% of injuries (Fig. 3). Women were more likely to report being assaulted by a partner or date ($\chi^2(1) = 22.6$; $p < 0.001$). Dates of injury and of first homelessness were available for 98 of the 100 participants in the TBI group. Of these, 58 (59.2%) reported their most severe injury before first becoming homeless or vulnerably housed, 2 (2.0%) during the same year, and 38 (38.8%) afterward (Fig. 3). Mental and physical health-related quality of life scores were poorer in participants with a self-reported TBI, whereas Charlson comorbidity scores did not differ (Table 1).

Adjusting for age and sex, logistic regression revealed that self-reported TBI was associated with ongoing neurological symptoms (headaches, dizziness, and memory complaints) and mood disorders (Table 2). Further, with the exception of headaches, neurological symptoms and mood disorders were more prevalent in those with self-reported moderate/severe TBI, suggesting a dose-response relationship. Whereas clinically diagnosed cognitive impairment was more frequent in the TBI group (see Table 1), ANCOVA analyses indicated that there were no statistically significant neurocognitive test differences between groups.

To investigate the relationship between mental health and mechanism of TBI, specifically assault, we dichotomized TBI mechanism into "assault-related" or "assault-unrelated." There was no association between TBI that was caused specifically by assault and the prevalence of any psychiatric diagnoses ($ps > 0.1$; see Supplementary Table 2 (see online supplementary material at <http://www.liebertpub.com>) for detailed comparisons).

Mood disorders, but not anxiety disorders, psychotic disorders, or suicidal ideation, were more prevalent in the TBI group (see Table 1). We examined the associations between mood disorders, self-reported TBI, and health-related quality of life. In addition to age, self-reported TBI, a current mood disorder, and their interaction were associated with lower SF-36 mental component scores (Table 3; Fig. 4). In contrast, only age and the Charlson comorbidity score were associated with SF-36 physical component scores (Table 3; Fig. 4).

Magnetic resonance imaging + traumatic brain injury

Evidence of trauma was detected in the MRI scans of 20 of 288 (6.9%) participants (MRI + TBI; see Fig. 2 for examples). Six of these participants had a self-reported history of moderate/severe TBI, whereas 5 were classified as mild based on self-report. TBI that is mild by clinical criteria, but that has evidence of neuroimaging abnormalities associated with the trauma is termed "complicated mild TBI."²¹ Four participants with MRI + TBI reported a head or face injury with no subsequent LOC or confusion, 3 did not report any history of head or face injury, and 2 could not be categorized because of an unknown length of LOC. Injury locations were temporal lobe only ($N = 10$), frontal lobe only ($N = 5$), temporal and frontal lobes ($N = 4$), and parietal lobe ($N = 1$; Fig. 5A). Demographic characteristics did not differ between the MRI + TBI and the matched no-TBI groups (see Supplementary Table 3) (see online supplementary material at <http://www.liebertpub.com>).

In contrast to self-reported TBI, participants with MRI + TBI had significantly lower scores for immediate memory ($t_{(59)} = 2.08$; $p = 0.042$; Cohen's $d = -0.568$) relative to their matched controls. Additionally, data patterns suggest potentially a more global

TABLE 1. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Characteristic	All (n = 205)		No-TBI (N = 105)		TBI (n = 100)		P value
	Mean	SD	Mean	SD	Mean	SD	
Age (years)	43.5	9.8	41.8	9.8	45.2	9.6	0.01
Age at injury					25.8	13.9	
Education (years)	10.3	2.2	10.1	2.0	10.5	2.4	0.22
Homeless duration (years) ^a	3.5	6.0	3.3	4.7	3.8	7.1	0.54
Marginal housing duration (years) ^b	7.6	7.9	7.2	7.2	7.9	8.6	0.55
Charlson comorbidity	3.4	3.0	3.2	3.1	3.7	3.0	0.19
SF-36 Mental component score	42.0	12.0	43.6	11.6	40.2	12.3	0.04
SF-36 Physical component score	44.6	10.4	46.2	9.5	43.0	11.0	0.03
	n	%	n	%	n	%	p value
Sex							0.33
Male	158/205	77.1	78/105	74.3	80/100	80.0	
Female	47/205	22.9	27/105	25.7	20/100	20.0	
Race/ethnicity							0.37
White	116/205	56.6	58/105	55.2	58/100	58.0	
Aboriginal	63/205	30.7	34/105	32.4	29/100	29.0	
Black	8/205	3.9	6/105	5.7	2/100	2.0	
Other	18/205	8.8	7/105	6.7	11/100	11.0	
Ever charged with a criminal offense	165/175	94.3	75/84	89.3	90/91	98.9	0.007
Current neurological							
Headaches	59/205	28.8	23/105	22.9	35/100	35.0	0.06
Dizziness/fainting	59/205	28.8	19/105	18.1	40/100	40.0	0.001
Self-reported memory problems	62/205	30.2	22/105	21.0	40/100	40.0	0.003
Seizure, lifetime	33/205	16.1	12/105	11.4	21/100	21.0	0.06
Infectious disease (active)							
HIV	35/203	17.2	19/105	18.1	16/98	16.3	0.74
Hepatitis C	100/199	50.3	51/101	50.5	49/98	50.0	0.94
Current mental illness							
Psychotic disorder	96/205	46.8	51/105	48.6	45/100	45.0	0.61
Mood disorder	62/205	30.2	23/105	21.9	39/100	39.0	0.008
Anxiety disorder	58/205	28.3	28/105	26.7	30/100	30.0	0.60
Post-traumatic stress disorder	15/205	7.3	5/105	4.8	10/100	10.0	0.15
Suicidal ideation	21/205	10.2	7/105	6.7	14/100	14.0	0.08
Clinical cognitive impairment	18/205	8.8	5/105	4.8	13/100	13.0	0.04
Substance dependence							
Stimulant, current	169/205	82.4	90/105	85.7	79/100	79.0	0.21
Opioid, current	95/205	46.3	48/105	45.7	47/100	47.0	0.85
Cannabis, current	62/205	30.2	30/105	28.6	32/100	32.0	0.59
Alcohol, current	36/205	17.6	18/105	17.1	18/100	18.0	0.87
Alcohol, lifetime	107/205	52.2	47/105	44.8	60/100	60.0	0.03

p values are based on Student's *t*-test or chi-squared differences comparing TBI versus No-TBI.

^a*N* = 201, no-TBI *N* = 103, TBI *N* = 98.

^b*N* = 203, no-TBI *N* = 104, TBI *N* = 99.

SF-36, Short-Form 36-item Health Survey; HIV, human immunodeficiency virus; SD, standard deviation; TBI, traumatic brain injury.

Italic = *p* < 0.05.

pattern of impairment given that cognitive performance scores on all other cognitive tests were generally higher in the matched No-TBI group relative to MRI + TBI participants (Cohen's *d* range: -0.157 to -0.443).

There was widespread reduced white matter integrity (indexed with FA) in the MRI + TBI group (Fig. 5B). Lower FA was global and bilateral, despite focal macroscopic radiological abnormality confined to one region in 16 participants and to two isolated regions in the other 4 participants.

Total cortical gray matter volume, as a percentage of total brain volume, was also lower in the MRI + TBI group relative to the matched No-TBI controls (27.0% vs. 28.5%; $t_{(58)} = 2.38$; $p = 0.021$; Fig. 5C). In addition, gray matter was lower even in areas remote

to the site of focal injury. Specifically, MRI + TBI participants exhibited lesser cortical gray matter volumes not only confined to the area of trauma-related encephalomalacia, but also when only uninjured cerebral lobes were analyzed. Uninjured frontal (10.2% vs. 11.0%; $t_{(49)} = 2.39$; $p = 0.021$) and occipital (2.9% vs. 3.1%; $t_{(58)} = 2.00$; $p = 0.050$) lobes showed lower gray matter volumes when a traumatic lesion was present in another part of the brain (Fig. 5D).

The relationships between cognitive function, total gray matter, and frontotemporal gray matter volumes were analyzed in the MRI + TBI group. Total cerebral gray matter volume was strongly correlated with performance on the Stroop color-word ($r = 0.73$; $p = 0.001$), HVLT immediate recall ($r = 0.50$; $p = 0.030$), and HVLT delayed recall ($r = 0.64$; $p = 0.003$) tasks, but not with the Rapid

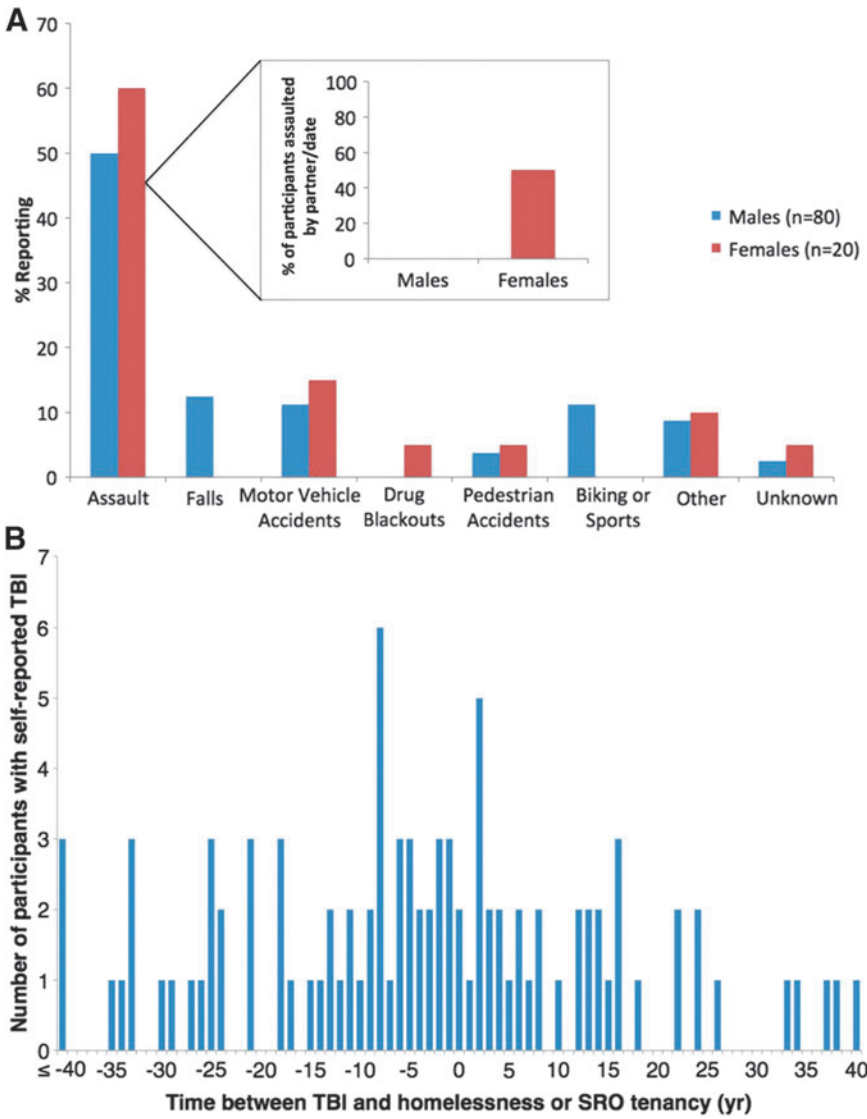


FIG. 3. Features of self-reported traumatic brain injury (TBI). (A) Cause of most severe TBI by sex. (B) Temporal relationship between onset of first homelessness or single-room occupancy (SRO) hotel housing and most severe TBI.

Visual Information Processing Task, the Intra-Dimensional-Extra-Dimensional Set Shift, or the Iowa Gambling Task. These correlations held when frontal and temporal lobes were analyzed independently. To test the association between white matter integrity and cognition, we specifically focused on the CC because it is a pathway

for multiple cognitive networks and is also the most commonly damaged white matter structure after TBI, as confirmed by post-mortem histology²² and DTI.²³ FA of the CC showed a strong correlation with both the Stroop color-word task ($r=0.722$; $p=0.002$) and the HVLIT delayed memory task ($r=0.527$; $p=0.024$).

TABLE 2. AGE- AND SEX-ADJUSTED ODDS RATIOS (95% CI) FOR SYMPTOMS ASSOCIATED WITH SELF-REPORTED TRAUMATIC BRAIN INJURY

TBI severity	N	Headaches		Dizziness		Memory complaints		Mood disorder	
		Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
None	105	1.0		1.0		1.0		1.0	
Mild	40	1.8 (0.8–4.1)	NS	2.4 (1.0–5.5)	0.044	1.7 (0.8–3.9)	NS	1.7 (0.8–3.9)	NS
Moderate/Severe	49	2.0 (1.0–4.3)	NS	3.6 (1.7–7.8)	0.001	2.9 (1.4–6.2)	0.004	3.1 (1.5–6.6)	0.003
All TBI	100 ^a	1.9 (1.0–3.6)	0.044	3.2 (1.7–6.3)	<0.001	2.4 (1.3–4.5)	0.006	2.4 (1.3–4.5)	0.006

^aIncludes 11 participants where LOC or memory loss/confusion was endorsed, but length of time was not recorded. CI, confidence interval; TBI, traumatic brain injury; NS, not significant.

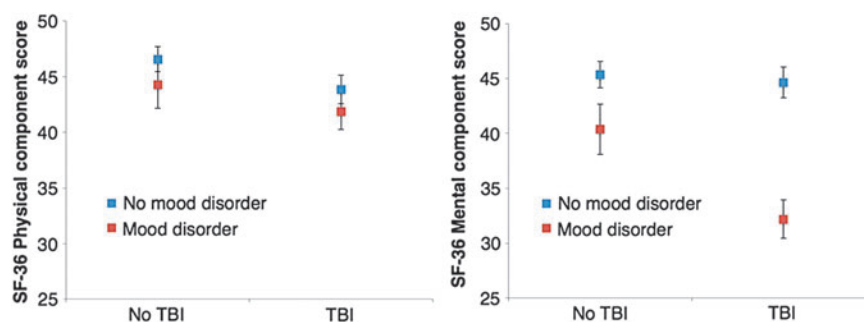


FIG. 4. Effect of self-reported traumatic brain injury (TBI) and mood disorders on physical and mental component SF-36 scores of health-related quality of life. SF-36, Short-Form 36-item Health Survey.

Discussion

In a community-based cohort of homeless or vulnerably housed participants, a history of TBI was common, consistent with reports from other homeless cohorts.⁴ We found a radiologically confirmed TBI rate of 6.9%. This is approximately 3 times the rate of 2.3% found in the general population.²⁴ A self-reported TBI history was associated with a higher prevalence of neurological symptoms and mood disorders, but not overall multi-morbidity. Mental health indices were significantly poorer in those with a self-reported TBI history, poorer in those with ongoing mood disorders, and the poorest in those with comorbid self-reported TBI and mood disorders. In those with MRI-confirmed TBI, local injury was associated with changes in remote cortical regions and white matter tracts. These trauma-associated structural MRI findings were associated with cognitive impairment.

Personal safety is a clear and unresolved issue for homeless and vulnerably housed people. Assault was overwhelmingly the most common cause of TBI in this cohort, in contrast to the general population in which assault is a minor cause.²⁵ It is also notable that among women in this cohort, TBI caused by assault was commonly perpetrated by a partner or date. The majority of participants (59%) reported their most severe TBI before first becoming homeless or vulnerably housed, similar to reports of 70–87% in other homeless cohorts.⁴ Participants who self-reported TBI were more likely to report persistent subjective somatic complaints, such as headaches, dizziness, and memory complaints, particularly those with moderate or severe injuries. This finding is reflected in the literature for both homeless and vulnerably housed cohorts as well as in the general population.^{26–28}

Although the broader substance abuse literature is mixed, previous studies related to homeless and vulnerably housed people have reported increased rates of substance abuse in individuals with TBI, including one study that also involved participants from Vancouver.^{4,26,29–31} None of these studies used objective testing to confirm substance use histories. Urine drug screens in the present study did not reveal differential substance use between participants with and without a self-reported TBI. In addition, rates of DSM-IV diagnoses made by psychiatrists were similar among participants with and without self-reported TBI, with the exception of alcohol dependence, which was higher in those with a history of self-reported TBI. An interesting observation by others that moderate and severe brain injuries, in particular, may actually decrease substance abuse³² could explain some of our null findings. Explanations include a reduced capacity of those with more serious injuries to obtain drugs, or apathy associated with TBI leading to a decrease in drug-seeking behavior.

In the general population, a history of TBI is associated with higher rates of depression, anxiety disorders, psychotic disorders, obsessive-compulsive disorder, substance dependence, suicide attempts, and lower quality of life.^{33,34} Four previous studies have reported higher rates of mental illness among homeless and vulnerably housed individuals with TBI,^{26,27,29,30} but did not report rates of specific disorders. We found an increased rate of mood disorders, consistent with existing TBI literature, but no association with psychosis, suggesting some specificity of TBI as a risk factor for mental disorders. In this cohort, mood disorders and self-reported TBI interacted with respect to poor health outcomes, and the prevalence of mood disorders was associated with severity of TBI. Mood disorders co-occurring with TBI have been associated with decreased

TABLE 3. MODELING SF-36 MENTAL AND PHYSICAL COMPONENT SCORES BY SELF-REPORTED TRAUMATIC BRAIN INJURY, MOOD DISORDERS, AND THE INTERACTION BETWEEN THESE PREDICTORS CONTROLLED FOR AGE, SEX, AND CHARLSON MULTIMORBIDITY SCORE

	SF-36 Mental component score			SF-36 Physical component score		
	F ^a	Effect size ^b	p value	F	Effect size	p value
Age	12.4	0.059	0.001	4.1	0.020	0.045
Sex	0.34	0.002	0.56	0.36	0.002	0.55
Charlson score	0.028	<0.001	0.87	4.7	0.023	0.032
TBI	6.9	0.034	0.009	1.5	0.008	0.22
Mood disorder	26	0.116	<0.001	2.4	0.012	0.12
TBI×Mood disorder	4.5	0.022	0.035	0.001	<0.001	0.97

^aF_(1,198) for all analyses.

^bEffect sizes are shown by the partial eta-squared (η_p^2) statistic.

SF-36, Short-Form 36-item Health Survey; TBI, traumatic brain injury.

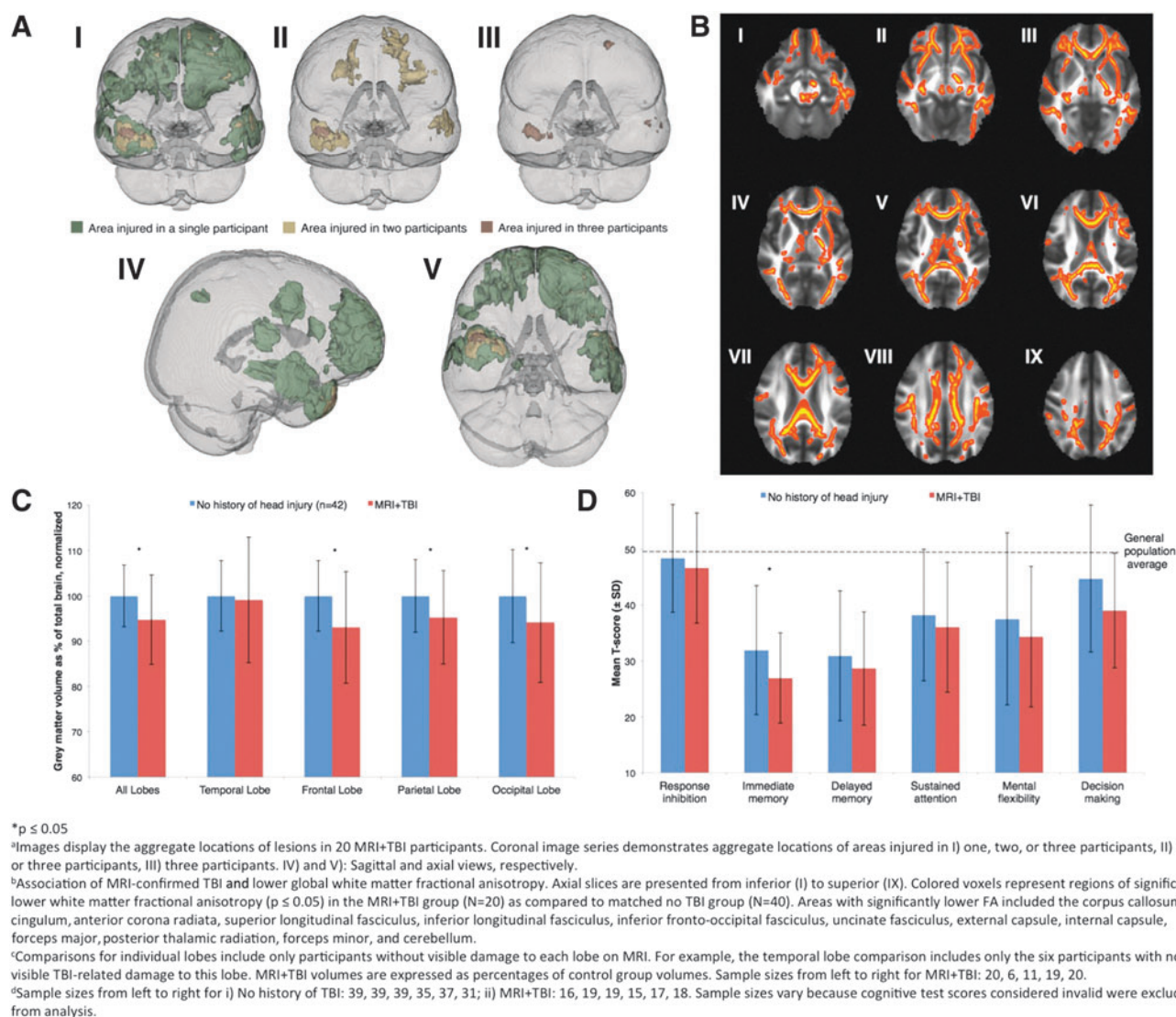


FIG. 5. Injury locations (A), white matter changes (B), cognitive effects (C), and gray matter changes in participants with evidence of trauma on MRI. MRI, magnetic resonance imaging; SD, standard deviation; TBI, traumatic brain injury.

substance abstinence rates,³⁵ impaired psychosocial functioning,³⁶ and higher unemployment rates.³⁷ The causal relationship between mood disorders and TBI remains uncertain and may be bidirectional, but most studies, including ours, support the conclusion that TBI is a risk factor and possible precipitant for mood disorders.³⁴

Circumstances surrounding the TBI may be just as relevant to the development of subsequent psychiatric disorders as the injury itself. These may be especially important if the mechanism of TBI is assault. In this sample, however, we found no differences in rates of psychiatric disorders between assault-related and -unrelated TBI. Reasons for this null finding could include the high level of physical and emotional stress encountered routinely by this population, and the almost universal drug use that may obscure symptoms required for neuropsychiatric diagnosis. There may also be a sex-assault interaction, but our sample size was too small to perform sex-stratified analysis because only 10 women reported an assault-related TBI.

Cognition in this sample did not significantly differ between those who did and did not self-report a TBI. Multiple studies in homeless and vulnerably housed cohorts have also found no asso-

ciation between self-reported TBI and cognition.^{38–40} More potent factors that impair cognition in this population (e.g., high rates of substance use, mental illness, viral infection, and childhood abuse) may mask the adverse neurocognitive sequelae of TBI, and a comprehensive accounting of all such factors in this heterogeneous population is difficult.

We did, however, find an association between cognition and those with MRI evidence of brain trauma. This was an expected finding given that the presence of traumatic lesions, even after mild TBI, predicts a poorer outcome.^{41,42} Further, although TBI is often conceptualized as localized injury, we found widespread reductions in both cortical gray matter volume and underlying white matter integrity in our MRI + TBI participants. There were also structure-function relationships in this cohort: Total gray matter volume, frontal and temporal gray matter lobar volumes, and corpus callosal integrity strongly correlated with cognition.

This study has a number of strengths. We characterized TBI in a large, community cohort of homeless and vulnerably housed individuals both subjectively with self-report and objectively with neuropsychological assessments and MRI. Psychiatrists and

neurologists evaluated all participants, and substance use was verified with urine samples, strengthening the validity of mental health and substance dependence diagnoses.

There are multiple limitations worthy of discussion. The first is the relatively small number of participants with MRI evidence of brain injury, which limited our statistical power and precluded investigations such as of other important questions, including, for example, the relationship between site of injury and type of neurocognitive impairment. Second, the subjective nature of ascribing an MRI abnormality to trauma is problematic. We addressed this by using multiple physicians skilled in MRI interpretation, but we cannot be certain that some of the lesions did not result from other pathologies, such as stroke. Third, we did not gather any temporal data in relation to health diagnoses, making causative inferences with regard to TBI difficult.

A final, but significant, limitation of this study is the accuracy of self-reporting TBI. In the general population, the vast majority of TBIs are mild, whereas in this sample almost half were classified as moderate/severe. Our ascertainment question, "Have you ever had a serious head/face injury?" by including the word *serious*, most likely led to an under-reporting of mild injuries. Also, if the participant had a history of mild TBI in addition to a more severe TBI, only the more severe injury would be reported. Our self-report TBI rate of 35.3% is therefore likely an underestimate, but this rate still represents a substantial increase when compared to existing studies in the general population that use analogous TBI ascertainment criteria.³³ Silver and colleagues, for example, found a TBI prevalence rate of 7.2% in a community sample when asking the similar question "have you ever experienced a severe TBI associated with loss of consciousness or confusion."³³

Compounding this issue, self-reporting TBI severity relies on an individual's memory at a time that memory is expected to be disrupted. In the absence of a corroborating witness, duration of LOC, for example, is impossible to disambiguate from duration of PTA given that one negates insight into the other. As such, some of our participants may have overestimated duration of LOC when, in reality, they were in a period of PTA. Together with the level of cognitive impairment in our participants and the potential for injuries affecting recall of the traumatic event to go unreported, these issues may explain why those 20 individuals with focal traumatic lesions on MRI spanned the entire self-report severity spectrum, with 3 reporting no history of any previous head or face injury and 4 reporting previous head or face injury, but without any LOC or PTA. This discrepancy underscores the need for a lower threshold to obtain neuroimaging in this population.

In summary, we found that TBI was associated with persistent somatic complaints, cognitive problems (i.e., MRI + TBI), and mood disorders in a group where these problems and illnesses were already common. TBI is associated with poorer mental health in this population, and this relationship persists after adjustment for comorbidities. Mood disorders appear to interact with TBI to produce disproportionately poor health outcomes and should be specifically evaluated when a history of TBI is suspected. The observation that over one third of participants with MRI evidence of trauma reported no clinical history of TBI suggests a lower threshold for imaging in people with psychiatric symptoms or disability who are homeless or vulnerably housed.

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William Honer has received consulting fees or sat on Advisory Boards for In Silico, Eli Lilly, Roche, Lundbeck, and Otsuka. Alasdair Barr has received consulting fees or sat on Advisory Boards for Bristol-Myers Squibb, Eli Lilly, and Roche. Ric Procyshyn has received speaking and Advisory Board fees from AstraZeneca, Bristol-Myers Squibb, Janssen, Otsuka, Pfizer, and Sunovion. William MacEwen has received speaking or consulting fees, or sat on Advisory Boards for Apotex, AstraZeneca, Bristol-Myers Squibb, Janssen, Lundbeck, Otsuka, Pfizer, and Sunovion and research grant support from Janssen. Alexander Rauscher has received Advisor Board fees from Hoffmann-La Roche. Thalia Field has received speaking or advisory board fees from Bayer Canada and Pfizer and research funds from Bayer Canada and Boehringer Ingelheim Canada. William Panenka has a practice in forensic neuropsychiatry and is a director of Abbatis bioceuticals, an early stage biotech company.

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