

Is bipolar disorder associated with traumatic brain injury in the homeless?

Esiste un'associazione fra disturbo bipolare e trauma cranico nei senzatetto?

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SUMMARY. Links between Bipolar Disorder (BD) and medical conditions are increasingly reported. Traumatic Brain Injury (TBI) is a prevalent medical condition found in homeless populations. **Aim.** This paper examines the correlation between the presence of BD and TBI, comparing homeless affected by Bipolar Disorder, Unipolar Depression (UD) and Schizophrenia Spectrum Disorder (SSD), controlled for other TBI risk factors such as age, gender, comorbid alcohol and substance use disorders as the confounding variables. **Methods.** From 489 participants of Vancouver arm of the At Home/Chez Soi Study, 416 homeless had psychiatric diagnoses, alcohol and substance dependence, and TBI determined by the MINI Questionnaire and the Comorbid Conditions List. 147 patients with BD were compared with 175 UD and 94 SSD for age, gender, the presence, number and severity of TBI and the presence of alcohol and substance use diagnosis, at a univariate and multivariate level. **Results.** The homeless with BD had higher percentage of TBI compared to the homeless with SSD. However, the reported severity and frequency of TBI by patients with BD, UD, and SSD were not statistically different. BD diagnosis was associated with TBI at multivariate level. **Conclusions.** TBI could be considered one of the physical burdens associated with BD in the homeless population.

KEY WORDS: bipolar disorder, traumatic brain injury, homelessness, schizophrenia, alcohol dependence, substance dependence.

RIASSUNTO. Sempre più frequentemente vengono riportate correlazioni fra disturbo bipolare (BD) e condizioni mediche generali; fra queste ultime, il Trauma Cranico (TBI) è una condizione prevalente nella popolazione dei senzatetto. **SCOPO.** L'articolo si prefigge di esaminare la correlazione fra BD e TBI, confrontando una popolazione di senzatetto affetti da BD, Depressione Unipolare (UD) a Psicosi di tipo Schizofrenico (SSD), escludendo quei fattori di rischio propri del TBI quali età, sesso, dipendenza da sostanze e da alcol, che potrebbero essere considerati come fattori confondenti. **METODO.** Dei 489 senzatetto partecipanti al gruppo di Vancouver dello studio At Home/Chez Soi, 416 hanno ricevuto una diagnosi di disturbo psichico, dipendenza da alcol e/o sostanze e trauma cranico, utilizzando il questionario MINI e la Checklist di Condizioni di comorbidità. Sono stati quindi confrontati, a livello univariato e multivariato, 147 soggetti affetti da BD, 175 affetti da UD e 94 affetti da SSD per le variabili di età, sesso, presenza, numero e severità di trauma cranico e diagnosi di dipendenza da sostanze e alcol. **RISULTATI.** I senzatetto affetti da BD presentavano una frequenza superiore di traumatismo cranico rispetto a quelli affetti da Psicosi di tipo Schizofrenico. Considerando invece la severità e la frequenza del TBI, non sono emerse differenze statisticamente significative fra i 3 gruppi di senzatetto. La diagnosi di BD si associava a TBI a livello multivariato. **CONCLUSIONI.** Il trauma cranico può essere quindi considerato come una delle condizioni fisiche che si associa al BD, nella popolazione di senzatetto.

PAROLE CHIAVE: disturbo bipolare, trauma cranico, senzatetto, schizofrenia, dipendenza da alcol, dipendenza da sostanze.

INTRODUCTION

Bipolar Disorder (BD) is increasingly reported to be associated with medical comorbidities. Growing evidence shows a significant increase in the medical burden among patients diagnosed with BD such as cardiovascular, respiratory¹, thyroid,

hepatic¹, neurological diseases², metabolic syndrome³, and injuries⁴. Anecdotally, in patients diagnosed with BD, the prevalence of all types of injuries, including accidents and related injuries, are reported to be higher than general population (40.9% Vs 20%, respectively)¹ contrasting to a lower reported lifetime prevalence of 11.9%⁵ and 13%⁴ in other studies. Brain

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injuries in particular among those with BD are reported to be 18.5% by Kemp et al⁶. Head injuries with unconsciousness have similar prevalence rates for BD amongst American and European population (15,1% vs 13,8%, respectively)⁷.

Traumatic Brain Injury (TBI) is a serious medical condition and a leading cause of death and permanent disability⁸ annually affecting 1.7 million people in the United States⁹. TBI can be defined as a «blow or jolt to the head or a penetrating head injury that disrupts the function of the brain»⁹. Current reported main risk factors for TBI are age, male gender, a lower socioeconomic status¹⁰, mental disorders¹¹, high alcohol blood concentration and substance abuse¹²⁻¹⁴. Mental disorders are reported to be a risk factors for TBI¹¹ and certainly an important cause of disability¹⁵ with reported increased diagnosis rate for mental disorders after TBI¹⁶⁻²⁰.

Focusing on homeless populations, TBI is one of the most frequent medical conditions²¹⁻²³ with a reported lifetime prevalence rate of 8% to 53%²²⁻²⁵ that is 5 or more times higher than in general population^{21,23,26}. Hwang and colleagues reported the highest TBI prevalence in the homeless at 53% with higher rate in men (58%) compared to women (42%)²¹. Homeless population also have high prevalence of mental disorders, including schizophrenia, affective²⁷⁻³³, and substance use disorders^{27,28,30,32}. Furthermore, homeless with a history of TBI have been reported to have significantly higher lifetime prevalence of different medical conditions, as well as substance use disorders (SUD) and mental disorders^{19,21,34}.

The aim of this study is to examine the association between BD and the presence of TBI, comparing homeless affected by either BD, Unipolar Depression (UD) or Schizophrenia Spectrum Disorder (SSD) while controlling for known risk factors for TBI: age, gender and substance dependence (including alcohol).

METHODS

Participants

The study sample is comprised of 497 participants. All participants were Canadian citizens of at least 19 years who met the criteria for absolute homelessness or precariously housed status and received a diagnosis of mental disorder according to Mini-International Neuropsychiatric Interview (MINI) at the time of study entry^{35,36}. Comorbid conditions including lifetime presence of TBI were screened using the Comorbid Condition List (CMC)³⁷.

The present report included 489 of 497 participants. Eight participants were missing mental disorder diagnosis and were excluded. For the present study we screened for the presence of BD, UD and Schizophrenic Spectrum Disorders at baseline evaluation, according to MINI diagnostics criteria, leading to a sample size of 416 homeless. This sample was characterized by a mean age of 39.93±10.8sd. 299 (71.9%) were male, 393 (94.5%) were living alone, 232 (55.8%) had a low educational level, 395 (95.0%) were unemployed and 61 (14.7%) were aboriginal.

The research study was conducted on data from the At Home/Chez Soi study, a 4-year randomized controlled trial, designed to test the effectiveness of Housing First for mentally ill homeless across five sites in Canada³⁵. The At Home/Chez Soi study was designed as a cross-sectional naturalistic and observational using a single evaluation of homeless psychiatric patients. The purpose of the present analysis is to estimate the associations

between demographic information, TBI, and BD, UD, SSD and Substance/Alcohol Dependence patients.

Informed Consent IRB approval

Research ethics board approval has been obtained from 11 institutions and a safety and adverse events committee is in place. Written informed consent was obtain by participants. The At Home/Chez Soi Study has been registered with the International Standard Randomised Control Trial Number Register and assigned ISRCTN42520374.

Procedures

For the purpose of the present study data were collected at the time of study entry. These variables were comprised in the following questionnaires:

Demographics, Service & Housing History (DSHH)

Age, marital status, housing situation, education, source of income, and social status were collected. Participants were also asked to identify the ethnic group/descent from the list of European/Caucasian, Aboriginal, African, Asian, Hispanic/Latin American, and Other. The Aboriginal peoples – Cree, Carrier, Dene – who participated in this study represented First Nations found throughout British Columbia³⁸.

Traumatic brain injury (TBI)

A self-reported lifetime history of TBI was assessed at baseline³⁷. Individuals with TBI were identified as those responding “yes” to the question: “Have you ever had an injury to the head which knocked you out or at least left you dazed, confused or disoriented?”. Participants were asked how many such injuries they had over their lifetime and whether the injury resulted in unconsciousness and the duration of unconsciousness. A mild TBI was defined as a head injury that left the person dazed, confused, or disoriented, but resulted in no unconsciousness or unconsciousness for less the 30 minutes. A moderate or severe TBI was defined as a head injury that resulted in unconsciousness for more than 30 minutes. These definitions are consistent with standardized consensus criteria³⁹. The same question has been already used in previous publications^{21,23,40}. Number of injuries were collected and classified into a new variable with “low-frequency of TBI” and “high-frequency of TBI” (more or equal to 5 injuries) on the bases of the mean scores. There was no information regarding the date of occurrence of the injury.

Mini-International Neuropsychiatric Interview (MINI)

Lifetime and current mental and SUD were diagnosed using the MINI Plus, version 6.0.0⁴¹. The MINI Plus has demonstrated reliability and validity as a structured clinical interview that is designed to assess Axis I SUD and mental disorders and Axis II antisocial personality disorder based on the diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV)⁴² and the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)^{41,43}.

UD, BD, and SSD (including schizophrenia, and non-affective psychosis) were determined with the MINI for current or past

episodes of depression, mania/hypomania and psychosis at the baseline. Alcohol dependence and substance dependence were diagnosed at study entry.

Analyses

Homeless with BD, UD and SSD were compared at univariate level with ANOVA test and Bonferroni corrected for multiple comparisons chi-square. Multinomial logistic regression was carried out considering diagnosis (SSD, BD, UD) as dependent variable (with SSD as reference diagnosis) controlled for other TBI risk factors; age, gender, alcohol and SUD as the confounding variables. All analyses were performed using SPSS 20.0.

no differences were observed regarding the presence of knocked out or unconsciousness, the severity of the trauma and the number of injuries experienced between the 3 groups.

The homeless with BD and UD were more frequently diagnosed with substance dependence compared to the homeless with a diagnosis of SSD. The homeless with BD show higher percentage of alcohol dependence compared to the other two groups (Table 1).

Logistic regression shows a statistically significant positive association of a diagnosis of BD with TBI, controlled for age, gender and substance dependence (Table 2).

RESULTS

The mean age of participants with BD was not statistically different from those with UD and SSD. Socio-demographic characteristics of the three groups such as living situation, education, occupation and ethnicity were not statistically different either. The influence of gender did not meet a statistical significance (Table 1).

The homeless with a diagnosis of BD and UD show a greater number of lifelong TBI compared with homeless with SSD. However if we consider the characteristics of TBI,

DISCUSSION

The main result of the present study was that individuals diagnosed with BD and to a lesser extent UD were associated with a higher prevalence of lifelong TBI compared to the homeless with SSD, after adjusting for TBI risk factors at multivariate level. The severity and frequency of trauma was not found to differ between groups.

The present study found a positive association between BD and TBI in the homeless population. Previous studies on non homeless populations focused on the prevalence of TBI in the medical history of BD individuals^{6,7}, others tried to

Table 1. Demographic and clinical characteristics of Bipolar Disorder, Unipolar Depressed and Schizophrenia Spectrum Disorder Homeless, in the Homeless, At Home/Chez Soi Study Vancouver 2009-2013 (N=416).

	Missing Data*	Schizophrenia Spectrum Disorder N=94	Bipolar Disorder N=147	Unipolar Depression N=175		
		M±sd (range)	M±sd (range)	M±sd (range)	F	p
Age		41.05±11.2 (19-67)	40.13±(10.4) (19-66)	39.17±10.8 (19-65)	0.97	0.379
		N (%)	N (%)	N (%)	Chi	p
Gender (male)		76 (80.9)a	98 (66.7)b	125 (71.4)ab	5.73	0.057
Living Situation (alone)		90 (95.7)a	138 (93.9)a	165 (94.3)a	0.40	0.818
Education (<9 years)		48 (51.1)a	77 (52.4)a	107 (61.1)a	3.58	0.167
Occupation (unemployed)		89 (94.7)ab	135 (91.8)b	171 (97.7)a	5.77	0.056
Ethnicity (Aboriginal)		8 (8.5)a	21 (14.3)a	32 (18.3)a	4.70	0.096
TBI		45 (47.9)a	113 (76.9)b	119 (68.0)b	21.94	<0.001
Being knocked out	144	35 (79.5)a	96 (85.7)a	102 (87.9)a	1.82	0.401
Severe TBI	218	21 (67.7)a	43 (52.4)a	44 (51.8)a	2.58	0.274
Number of TBI per person (high frequency)	138	9 (20.0)a	39 (34.5)a	39 (32.5)a	3.29	0.192
Substance Dependence Diagnosis	17	34 (38.2)a	97 (69.3)b	107 (62.9)b	23.17	<0.001
Alcohol Dependence Diagnosis	38	15 (17.6)a	44 (32.6)b	46 (29.1)ab	6.04	0.049

* due to absence of responsiveness to questions.

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Table 2. Association of BD and UD with TBI, controlled for age, gender, diagnosis of Alcohol and Substance Dependence, compared with Schizophrenia Spectrum Disorder homeless.

Diagnosis §	Beta	Odds ratio	Min	Max	p
Bipolar Disorder					
Substance Dependence Diagnosis	1.290	3.63	1.95	6.77	<0.001
TBI	1.188	3.28	1.75	6.16	<0.001
Gender (male)	-0.991	0.37	0.18	0.74	0.005
Age	0.011	1.01	0.98	1.03	0.444
Alcohol Dependence Diagnosis	0.541	1.71	0.84	3.51	0.138
Unipolar Depression					
Substance Dependence Diagnosis	0.973	2.64	1.48	4.71	0.001
TBI	0.726	2.07	1.17	3.66	0.013
Gender (male)	-0.551	0.57	0.29	1.13	0.111
Age	-0.001	0.99	0.97	1.02	0.923
Alcohol Dependence Diagnosis	0.366	1.44	0.72	2.88	0.300

Statistic: chi square 49.058 df=10 p<0.001
 § Considering Schizophrenia Spectrum Disorder as reference diagnosis

shed light on the temporal relationship between TBI and mental illness, and BD has been found as one of mental disorders diagnosed after TBI⁴⁴⁻⁴⁶. The lack of clarity of causality between TBI and BDs is likely due to the paucity of data on the reported time of TBI onset in relation to time of BD diagnosis¹¹. The higher rates of accidents and injuries in BD, 40.9% Vs 20.0% in general population¹, could be explained by personality traits such as impulsivity⁴⁴. In this light, a recent review of Topolovec-Vranic suggested that impulsivity may play a role to predispose individuals to TBI²². As such, impulsivity with its four components (urgency; lack of premeditation; lack of perseverance; sensation seeking) and the impulse control disorder would not only be all common comorbidities⁴⁷ but also a core feature of the different phases of the illness⁴⁸ and a stable trait in BD⁴⁹⁻⁵¹. Impulsivity, risk-taking, sensation-seeking and low risk perception have been associated with BD^{47,48,51-53} and intentional, unintentional and repeated injuries⁵⁰. While the risk of TBI could be higher in the homeless due to the higher reported risk taking behaviours in the homeless population⁵⁴, a diagnosis of BD in a homeless person can be added to the risk of TBI through the impulsivity component of BD. The fact that impulsivity can be a common feature of all reported predictors of TBI (male gender, BD and alcohol dependence), this leads us to ponder the key role of this personality trait in leading to TBI.

Substance use was also found to be associated with BD; latest theories consider the whole spectrum of BD and substance use in a unitary perspective^{47,55-62}. Such complex entangled association can be explained by evidence reporting that in patients diagnosed with BD, impulsive behaviour and risk-taking behaviours may act as a common pathway for psychiatric comorbidities such as substance abuse^{60,63-65}, as well as physical comorbidities such as infections^{4,66} and obesity⁶⁷.

TBI was found to have a significant association with substance use as well, even if it is more often reported to be the consequence of substance use, rather than the cause^{19,68}. Horner showed that substance use after TBI could be often predicted by a pre-existing substance use/abuse⁶⁹. While anecdotal evidence hints on the causality of TBI for substance use disorder⁷⁰, especially in intoxication phase^{70,71}, Rogers' study failed to prove any causality of TBI for substance use, either¹⁹.

It is clear that the relationships between TBI, BD and substance use are complex. Results from the present study are of interest because of the finding that TBI was found to be positively associated with BDs and, to a lesser extent, UD even if when multivariate level substance dependence is taken into account as a confounding variable.

Additionally this study showed that the homeless population of our study diagnosed with SSD had a lower percentage of TBI compared to the homeless with BD and UD, and negative association in regression analysis. The association between schizophrenia or psychosis and TBI have been reported as controversial. The result of our study is supported by previous research that showed schizophrenia was not strongly associated with TBI⁴⁴ and the risk of developing schizophrenia was not increased after head injury⁷² not even after a severe TBI, followed over a maximum of 4.9 years^{16,20}. On the contrary, other studies reported head injury being a risk factor to develop schizophrenia⁷³⁻⁷⁵ or psychosis^{16,76}. Davison and Bagley⁷⁷ reported an increased prevalence of schizophrenia compared to general population by two to three fold over 10-20 years after TBI, later supported by Gualtieri⁷⁸ and Achte who reported that 7.6% of their participants with TBI developed chronic psychotic and delusional disorder⁷⁶. Moreover, a family study showed a possible

role of a mild childhood head injury in the expression of schizophrenia in families with genetic predisposition⁷⁹. The first meta-analysis on this topic was published in 2011, reporting a 60% risk of schizophrenia following TBI, especially among those with an inherited vulnerability for schizophrenia⁸⁰. Despite several studies emphasizing the comorbidity between TBI and schizophrenia, the specific nature of this relationship still remains unclear. Lastly, we should take into account that the lower percentage of SSD patients found with TBI in our study could also be related to presence of a mental health system having a greater capability to “capture” individuals with schizophrenia so they were less likely to become homeless.

LIMITATIONS

TBI was assessed through self-report data using the standardized Comorbidity List Questions for TBI used in the At Home/Chez Soi study. Unfortunately medical records of participants of the At Home/Chez Soi were not available to us at the time of the current study. Comorbidities List in At Home Study has no questions on the collection of information regarding the onset of the reported head injury in relation to the first time of diagnosis with BD, so the association of BD and TBI could not be furthered to any temporal association in current study. Further studies with more comprehensive questionnaires are recommended to investigate the temporal relationship of TBI and BD.

CONCLUSIONS

In summary, current study shows a statistically significant positive association between BD and TBI and substance dependence in the homeless, leading to the suggestion of TBI being a part of the medical burden of BD in this population. Such evidence could be a useful tool for clinicians for the identification of TBI in patients diagnosed with mental disorders as well as a lower threshold on treatment approaches for delivering a standard of care. Further studies are required to collect data on the temporal relationship of onset of TBI and the diagnosis of BD investigating if BD could predispose to TBI.

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