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Depression Strongly Influences Postconcussion Symptom Reporting Following Mild Traumatic Brain Injury

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Objective: To examine the influence of depression on postconcussion symptom reporting in patients following mild traumatic brain injury (MTBI). **Participants:** Sixty patients referred to a specialty clinic following MTBI, 58 outpatients with Structured Clinical Interview for *DSM*-diagnosed depression, and 72 healthy community control participants. **Procedure:** Participants with MTBI were divided into 2 subgroups on the basis of self-reported symptoms of depression (23 MTBI-depressed, 37 MTBI-not depressed). All participants completed a postconcussion symptom questionnaire. **Main outcome measure:** British Columbia Post-concussion Symptom Inventory. **Results:** There were significant differences in total reported postconcussion symptoms among all 4 groups (all $P < .002$; Cohen's $d = 0.68–3.24$, large to very large effect sizes; MTBI-depressed > depressed outpatients > MTBI-no depression > healthy controls). There were significant differences in the number of symptoms endorsed ($P < .05$), with the highest number of symptoms endorsed by the MTBI-depressed group, followed by depressed outpatients, MTBI-no depression, and healthy controls. **Conclusions:** Patients who experience MTBIs and who have a postinjury recovery course complicated by significant depression report more postconcussion symptoms, and more severe symptoms, than (*a*) outpatients with depression, and (*b*) patients with MTBIs who do not have significant symptoms of depression. **Keywords:** *depression*, *mild traumatic brain injury*, *postconcussion symptoms*

STRUCTURAL, microstructural, and functional imaging studies have not clearly established a causal link between persistent postconcussion symptoms and acquired brain damage following mild traumatic brain injury (MTBI).[1–4] Moreover, researchers have identified many other factors that can cause, maintain, or worsen postconcussion symptom reporting. A number of studies have clearly demonstrated that postconcussion symptoms are not specific to MTBI and are commonly reported in healthy adults[5–7] and in various clinical groups who have not sustained an injury to the brain.[8–13] Similarly, postconcussion symptom reporting is believed to be associated with premorbid personality characteristics[14–16] and is greatly influenced by the method by which the clinician elicits and documents symptoms; that is, interview versus questionnaire.[17] In addition, a number of social-psychological factors are believed to influence postconcussion symptom reporting, such as the nocebo effect,[18] "expectation as etiology,"[6,19,20] "diagnosis threat,"[21,22] and "good old days" bias.[19,23] As such, when considering a diagnosis of postconcussion syndrome, it is imperative for clinicians to systematically evaluate and eliminate the possible contribution of many different factors that may *cause or maintain* self-reported symptoms following MTBI (see Iverson and colleagues[24,25] for a more complete discussion).

One of the most clinically pervasive, and perplexing, differential diagnoses for the postconcussion syndrome is depression.[26,27] Depression is common following traumatic brain injuries of all severities[28,29] and can have multiple causes. Theoretically, it can relate to the neurobiological consequences of the injury, psychosocial factors, or both. Conceptually and theoretically, a depression spectrum disorder following MTBI, whether caused by neurobiological factors, psychosocial factors, or both, could be one type of postconcussion syndrome (if we assume that the syndrome can arise from different and interacting causes). Depression can also arise de novo, because of a combination of genetic predisposition and adverse life events, at some point following an MTBI.

There are 4 primary reasons why depression represents one of the most challenging differential diagnoses for the postconcussion syndrome. First, many of the

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diagnostic symptoms of depression, and other problems associated with this condition, are similar to the current definition of *postconcussion syndrome*. The diagnostic criteria for major depression include diminished ability to think or concentrate, indecisiveness, fatigue or loss of energy, and sleep problems.[30(p327)] In addition, major depression often is associated with irritability, excessive worry over one's health, and headaches.[30(p323)] Common lifestyle and psychosocial problems include strained social relationships, marital and family distress, occupational problems, academic problems, and substance abuse.[30(p323)] Therefore, it can be extremely difficult to determine whether a person's self-reported symptoms are due to depression, a persistent postconcussion syndrome, or both, because of the considerable symptom overlap in these conditions.

Second, depression is common with conditions that often coexist with MTBI. Cooccurring conditions may be physical injuries that are secondary to the MTBI itself (eg, soft-tissue or orthopedic injuries), psychological consequences of the injury experience (eg, posttraumatic stress disorder), or they may exist premorbidly (eg, substance abuse). Researchers have reported that depression is common in patients with chronic pain,[31,32] general trauma,[33] chronic headaches[34,35] posttraumatic stress disorder,[36,37] and substance abuse problems.[38,39] Therefore, the underlying cause of depression in the presence of these comorbidities can be very difficult, if not impossible, to determine.

Third, depression is one of the most common mental health problems in the world. The average age of onset is in the mid-20s, with an estimated lifetime risk in community samples ranging from 10% to 25% for women and 5% to 12% for men.[40–44] A single episode of major depression places an individual at greatly increased risk for a future episode, with estimates of recurrence ranging from 50% to 80%.[42,45–48] People who have had 2 or more episodes of depression are at extremely high risk for a future episode.[45] Therefore, the underlying cause of depression, in any given person at any given time, can be very difficult, if not impossible, to determine.

Fourth, patients with depression are expected to have cognitive complaints. Perceived cognitive impairment is a cardinal feature of depression.[49,50–52] Researchers have also reported that patients with depression perform more poorly on neuropsychological testing.[53] However, to our knowledge, no study has shown that the cognitive effects of depression can be accurately differentiated from the cognitive effects of an MTBI. The problem for clinicians and researchers is that a person with depression is virtually guaranteed to meet diagnostic criteria (ie, symptom complaint criteria) for a postconcussion syndrome,[54] regardless of whether that person (*a*) has ever injured his or her brain or (*b*) a past brain injury is causally related to his or her current symptoms.

The purpose of this cross-sectional study is to try to isolate and examine the depressive experience in a cohort of patients following MTBI by comparing MTBI patients with and without depression to depressed outpatients and healthy controls. It was hypothesized that both MTBI and depression would be associated with high levels of postconcussion-like symptom reporting; however, depression would have a more significant impact on symptom reporting than MTBI alone. More specifically, it was hypothesized that (i) patients with MTBIs with and without depression would report more symptoms than healthy controls; (ii) MTBI patients with depression would report more postconcussion symptoms than MTBI patients without depression; (iii) depressed outpatients would report more symptoms than healthy controls and MTBI patients without depression; and (iv) symptom reporting between MTBI with depression and depressed outpatients would be comparable.

METHODS

Participants

Participants were 190 community-dwelling adults from Vancouver, British Columbia, Canada. They composed 3 groups: individuals with MTBI ($n = 60$), outpatients with depression ($n = 58$), and healthy community controls ($n = 72$).

The participants in the MTBI sample (60.0% male) were selected from a larger sample of 110 consecutive referrals (January 2007 to September 2009) to a specialty clinic at GF Strong Rehab Center, Vancouver, British Columbia, Canada. This is a hospital-based "early intervention" clinic designed to provide educational services regarding the expected symptoms and recovery trajectory following a traumatic brain injury (primarily MTBI). Patients were included in the sample if (*a*) they had sustained a MTBI (88.1% of total sample), (*b*) English was their first language, or they had sufficient English fluency to complete the interview and questionnaires (97.3% of total sample), (*c*) they had been evaluated within 8 months of injury (98.2% of total sample), and (*d*) could be placed into 1 of 2 depression classifications outlined below (64.5% of total sample). A total of 60 patients met all criteria. For many patients, complete medical records were not available for review. For these patients, classification of MTBI was based on (*a*) self-reported loss of consciousness (LOC) and posttraumatic amnesia (PTA), and (*b*) self-reported injury information (eg, witnessed LOC, mechanism of injury).

The mean age and education of the MTBI sample was 36.0 years (SD = 13.1) and 14.2 years (SD = 1.9), respectively. Ethnicity of the sample was predominantly white (76.7%), with 10.0% Asian, 3.3% East Indian, 1.7% Canadian aboriginal, and 8.4% of other ethnic origins. The breakdown regarding LOC and PTA was as

follows: LOC: 83.3% positive, 8.3% negative, and 8.3% equivocal; PTA: 76.7% positive, 20.9% negative, and 3.3% equivocal. Glasgow Coma Scale (GCS) scores were not available for half of the patients (53.3%). Of the remaining sample, GCS = 15 (11.7%), GCS = 14 (30.0%), and GCS = 13 (5.0%). Day-of-injury CT scan intracranial abnormalities: 36.7% negative, 25.0% positive, 38.3% no CT scan undertaken at the time of injury. All patients were evaluated within 8 months following their injury (M = 51.8 days, SD = 61.1, range = 2–250 days). The breakdown of time post injury prior to evaluation was as follows: 0 to 1 month = 53.3%, 1 to 2 months = 25.0%, 2 to 3 months = 8.3%, and 3 or more months = 13.3%.

The 58 outpatients with depression were initially diagnosed and then referred by their psychiatrist or family physician. They were then administered the Structured Clinical Interview for *DSM-IV* (SCID-I). The SCID-I is a semistructured clinical interview used to establish *DSM-IV* Axis I diagnoses. The version of the SCID-I used in this study was the nonpatient research version 2.0, August 1998 revision.[26] All patients in the "depressed" group had an SCID diagnosis of major depressive disorder (92%), dysthymic disorder (5%), or depressive disorder NOS (3%). The diagnoses of the clinicians (ie, family physician or psychiatrist) corresponded to the diagnoses derived from the SCID-I interview the majority of the time. Specifically, the clinicians and the SCID raters agreed on a diagnosis of major depressive disorder in 81% of the cases. The clinicians diagnosed dysthymic disorder in 8 patients, but the SCID rater diagnosed major depressive disorder in 7 of these. In 3 instances, the SCID rater diagnosed dysthymic disorder, but the clinician diagnosed major depressive disorder in 2 of these cases. Thus, in approximately 18% of the patients, there was diagnostic disagreement between the SCID rater and the clinician. Nonetheless, all patients were diagnosed independently by both a physician and the SCID examiner as having a depressive disorder. Thirteen of the 58 patients reported a history of concussion or traumatic brain injury with LOC at some point in their lives. There was no significant difference on the total score derived from the postconcussion scale between those with (M = 22.5, SD = 12.6) and those without (M = 20.5, SD = 10.2) a history of self-reported concussion ($P < .55$). Therefore, to increase the heterogeneity and generalizability of the sample, these subjects were retained. This patient sample has also been used in a previous study.[23]

The healthy control group consisted of 72 adult participants in a study conducted in the community as part of a clinical trial in psychiatry (age: M = 49.9, SD = 11.7; education: M = 14.6, SD = 2.8; 59.5% female). These participants were screened for mental health, substance abuse, or neurological problems through the use of questionnaires and by administering the SCID. This control sample has also been used in previous studies.[5,25,55]

Measures

The British Columbia Post-concussion Symptom Inventory[25] (BC-PSI) is a 16-item measure designed to assess the presence and severity of postconcussion symptoms.[56] The BC-PSI is based on International Classification of Diseases-10 (ICD-10)[45] criteria for postconcussional syndrome and requires the test taker to rate the frequency and intensity of 13 symptoms (ie, headaches, dizziness/light-headedness, nausea or feeling sick, fatigue, sensitivity to noises, irritability, sadness, nervousness/tension, temper problems, poor concentration, memory problems, reading difficulty, and sleep disturbance) as well as the effect of 3 co-occurring life problems on daily living (ie, greater present vs past effects of alcohol consumption, worrying and dwelling on symptoms, and self-perception of brain damage). The 3 life problems are rated on a scale from 1 to 5, where 1 = "not at all" and 5 = "very much." The 13 symptoms are rated on a 6-point Likert-type rating scale that measures the frequency (ie, "how often") and intensity ("how bad") of each symptom in the past 2 weeks. Frequency ratings range from 0 (not at all) to 5 (constantly). Intensity ratings range from 0 (not at all) to 5 (very severe problem). To score the BC-PSI, the 2 ratings are multiplied together (how often × how bad) to create a single score for each item. These product-based scores are then converted to item scores that reflect both the frequency and intensity of symptom endorsement (range = 0–4). The participants' ratings of the 13 symptoms were the focus of this study. Item scores on the 13 individual symptoms range from 0 to 4. Item scores of 1 or more are classified as symptoms endorsed at a "mild level or greater." Item scores of 3 or more are classified as symptoms endorsed at a "moderate level or greater." Total scores are obtained by summing the scores on the 13 individual symptoms (range = 0–52).

The British Columbia Major Depression Inventory–Second Edition[57] (BC-MDI-II) is a 19-item questionnaire patterned specifically after the *DSM-IV* for major depressive disorder. The BC-MDI was designed to be more sensitive to the evaluation of clinically significant symptoms of major depression than other depression inventories, because of its ability to assess not only for the presence and severity of depressive symptoms but also their impact on a person's everyday life. This feature is critical to the evaluation of major depressive disorder because an essential *DSM-IV* criterion for assigning the diagnosis is evidence of disruption in daily activities as a consequence of depressive symptoms. The first 16 items of the BC-MDI-II are rated on a 5-point (1–5) Likert-type rating scale that measures the severity ("how

TABLE 1 *Descriptive statistics and ANOVA/χ^2 results[a] for demographic and injury severity variables by group (N = 190)*

	MTBI no depression ($n = 37$)		MTBI depressed ($n = 23$)		Healthy controls ($n = 72$)		Depressed outpatients ($n = 58$)	
	M	**SD**	***M***	**SD**	***M***	**SD**	***M***	**SD**
Age, y	34.8_1	13.7	37.8_2	12.1	$49.7_{1,2,3}$	11.7	41.2_3	12.6
Education, y	14.2	1.7	14.1	2.4	14.7	2.8	14.5	3.3
Days tested postinjury	42.7	50.1	66.4	74.5	...	...	...	...
	n	**%**	***n***	**%**	***n***	**%**	***n***	**%**
Gender (male)	24	$64.9_{1,2,3}$	12	52.2_1	30	41.7_2	17	29.3_3
Ethnicity (white)	28	75.7	18	78.3	...	...	...	...
LOC (positive)	29	78.4	21	91.3	...	...	...	...
PTA (positive)	28	75.7	18	78.3	...	...	...	...
MOI (MVA)	30	81.1	15	65.2	...	...	...	...
CT (intracranial abnormality)[b]	11	29.7	4	17.4	...	...	...	...

Abbreviations: CT, day-of-injury computed tomography scan; LOC, presence/absence of loss of consciousness; MOI, mechanism of injury; MTBI, mild traumatic brain injury; MVA, motor vehicle accident; PTA, presence/absence of posttraumatic amnesia.
[a]Values with the same subscript numerals are significantly different.
[b]Percentages were calculated on the basis of the entire sample, including those patients who had no CT scan undertaken at the time of injury.

bad") of each symptom over the past 2 weeks. The last 3 items measure the impact of these symptoms and problems on day-to-day life with regard to (*a*) their effectiveness at work or school, (*b*) family relationships and responsibilities, and (*c*) social life and recreational activities.

Procedure

The MTBI group was divided into 2 depression subgroups (23 MTBI-depressed, 37 MTBI-no depression) based on selected items from the BC-MDI-II.* These items were considered hallmark symptoms of depression that were least likely to overlap with postconcussion symptoms: (*a*) Sadness ("I feel sad, down in the dumps, and or blue; nearly every day"), (*b*) Guilt ("I am burdened by guilt"), (*c*) Worthlessness ("I feel worthless or useless"), (*d*) Thoughts of dying ("I often thinking about dying; most days"), and (*e*) Suicide ("I think about killing myself"). Patients were classified in the MTBI-no depression group if they met either of these 2 criteria: (*a*) all 5 symptoms were reported as absent, or (*b*) scores on Sadness < 2 (very mild problem) and guilt < 3 (mild problem) and worthlessness < 3 and thoughts of dying < 2 *and* Suicide = absent. Patients were classified in the MTBI-depressed group if they met any of these 4 criteria: (1) score of 4 (severe problem) or greater on sadness, (2) score of 3 (moderate problem) or greater on sadness and score of 3 or greater on 2 remaining symptoms, (3) score of 2 (mild problem) or greater on sadness and score of 2 or greater on 3 remaining symptoms, or (4) score of 3 or greater on sadness and score of 3 or greater on 1 remaining symptom. In other words, patients in this group needed to endorse a significant problem with sadness and other core depressive symptoms. Patients who did not fit these subgroup criteria were not included in the final sample (35.5% of consecutive sample).*

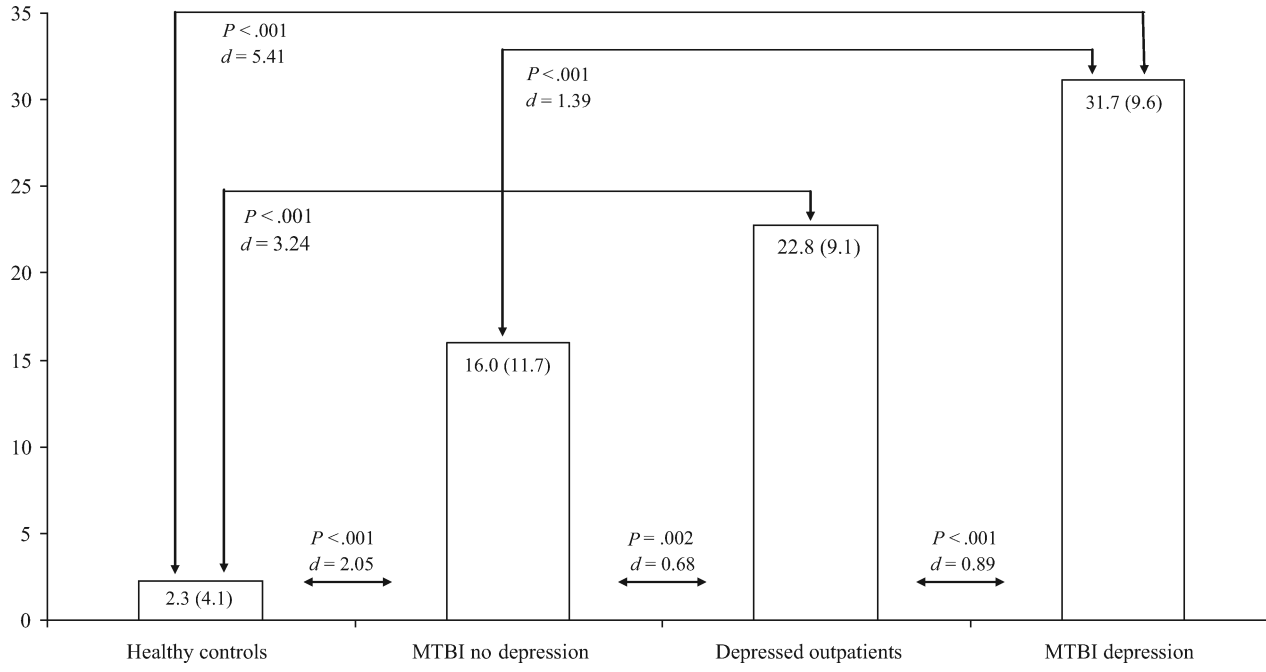
*It would have been our preference to classify these groups using the SCID. However, the SCID was not administered to the MTBI group.

RESULTS

Demographic and injury severity variables

Demographic characteristics for the 4 groups are presented in Table 1. There were significant main effects across the 4 groups for age ($F = 13.930$, $P < .001$) and gender ($\chi^2 = 12.411$, $P = .006$), but not for education ($F = 0.411$, $P = .745$). The Tukey post hoc analyses revealed that the healthy control group was significantly older than the other 3 groups ($P < .001$ for all comparisons). There were no significant differences

*The mean BC-PSI total score for this excluded group was 27.9 (SD = 9.3). This is significantly greater (ie, Mann Whitney *U* tests) than the control group without depression ($P < .001$, $d = 4.70$) and the MTBI-no depression group ($P < .001$, $d = 1.11$). However, there was no significant difference between this group and the depressed outpatients ($P = .056$, $d = 0.55$) or the MTBI-depression group ($P = .166$, $d = 0.34$). It is notable, however, that this excluded group had average BC-PSI total scores that were in between the depressed outpatient sample and the MTBI depressed group.



MTBI, mild traumatic brain injury.
Mild TBI not depressed ($n = 37$); Mild TBI depressed ($n = 23$); Healthy community controls, ($n = 72$); Depressed outpatients ($n = 58$).

Figure 1. Mann-Whitney *U* tests and Cohen's effect sizes for British Columbia Post-concussion Symptom Inventory total scores by group.

in age between the remaining groups. For gender, the MTBI-no depression group had a significantly higher proportion of men than both the depressed outpatient ($\chi^2 = 11.640$, $P < .001$) and the healthy control group ($\chi^2 = 5.262$, $P = .022$). There were no other significant group differences with respect to gender.

Given the known influence of some demographic variables on postconcussion symptom reporting,[26,27] the influence of age and gender on symptom reporting was examined in each group separately using Pearson product-moment correlations (for age) and analysis of variance (for gender). There were no significant correlations between postconcussion symptoms (ie, BC-PSI total scores) and age in all 4 groups: healthy controls ($r = -0.19$, $P = .118$); depressed outpatients ($r = -0.20$, $P = .125$); MTBI-depressed ($r = 0.28$, $P = .197$); MTBI-no depression ($r = 0.21$, $P = .207$). Similarly, there were no significant differences in postconcussion symptoms by gender in all 4 groups: healthy controls ($F = 1.774$, $P = .187$); depressed outpatients ($F = 0.091$, $P = .764$); MTBI-depression ($F = 0.115$, $P = .737$); MTBI-no depression ($F = 0.643$, $P = .428$).

Injury severity characteristics for the MTBI-depressed and MTBI-no depression groups are also presented in Table 1. There were no significant differences between the MTBI-depressed and MTBI-no depression groups for days tested postinjury ($P = .145$), ethnicity ($P = .582$), presence of LOC ($P = .426$), presence of PTA ($P = .127$), mechanism of injury ($P = .168$), or the presence of intracranial abnormalities on day-of-injury CT scans ($P = .452$; although there was a notable difference in percentages with abnormal scans: MTBI-no depression = 36.7% vs MTBI-depressed = 20.0%). Comparisons for GCS score were not undertaken because of the large amount of missing data (53.3% of sample with no GCS scores).

Postconcussion symptoms

Descriptive statistics, group comparisons (nonparametric due to nonnormal distributions), and Cohen's effect sizes for the BC-PSI total score across all groups are presented in Figure 1. There were significant main effects across the 4 groups for the BC-PSI total score (Kruskal-Wallis *H* test; $\chi^2 = 125.274$, $P < .001$). Post hoc analyses (using Mann-Whitney *U* tests) revealed significant differences (all $P < .002$) and large to very large effect sizes (range, $d = 0.68$–3.24) for all group comparisons. The highest total score was found for the MTBI-depressed group, followed by the depressed outpatient, MTBI-no depression, and healthy control group (ie, MTBI-depressed > depressed outpatients > MTBI-no depression > healthy controls).

The percentages of participants endorsing each of the 13 individual symptoms as "mild or greater" (ie, item scores of 1 or more) and "moderate or greater" (ie, item

TABLE 2 *Percentage of endorsed symptoms on the BC-PSI by group*[a]

	Mild or greater symptom rating[b]				Moderate or greater symptom rating			
BC-PSI items	**MTBI depressed**	**Depressed outpatient**	**MTBI no depression**	**Healthy controls**	**MTBI depressed**	**Depressed outpatient**	**MTBI no depression**	**Healthy controls**
Headache	91.3	62.1	70.3	23.6	69.6	29.3	45.9	4.2
Dizziness	91.3	34.5	59.5	9.7	43.5	12.1	24.3	0
Nausea	69.6	43.1	29.7	11.1	30.4	12.1	8.1	0
Fatigue	95.7	93.1	64.9	23.6	69.6	62.1	37.8	2.8
Sensitive to noise	82.6	55.2	51.4	5.6	65.2	20.7	27.0	1.4
Irritable	91.3	81.0	51.4	6.9	52.2	39.7	29.7	4.2
Sad	87.0	84.5	27.0	5.6	56.5	62.1	8.1	0
Nervous/tense	95.7	72.4	27.0	8.3	60.9	39.7	13.5	0
Temper problems	65.2	41.4	24.3	11.1	21.7	17.2	16.2	1.4
Poor concentration	87.0	86.2	56.8	1.4	65.2	51.7	32.4	0
Memory problems	82.6	77.6	56.8	9.7	47.8	46.6	32.4	1.4
Difficulty reading	73.9	44.8	35.1	2.8	34.8	25.9	21.6	0
Poor sleep	87.0	84.5	62.2	18.1	60.9	58.6	37.8	2.8
Total[c]	$95.7_{1,4}$	$94.8_{2,5}$	$62.2_{1,5,6}$	$8.3_{2,4,6}$	$91.3_{1,4}$	$79.3_{2,5}$	$40.5_{1,5,6}$	$4.2_{2,4,6}$

Abbreviations: BC-PSI, British Columbia Post-concussion Symptom Inventory; MTBI, mild traumatic brain injury.
[a]Mild TBI not depressed ($n = 37$); Mild TBI depressed ($n = 23$); Healthy community controls, ($n = 72$); Depressed outpatients ($n = 58$).
[b]Item scores of 1 or more = mild or greater; 3 or more = moderate or greater.
[c]For the total score, the percentages of each sample with scores of 10+ and 15+ in the "mild" and "moderate" columns respectively. Values with the same subscripts are significantly different ($P < .05$).

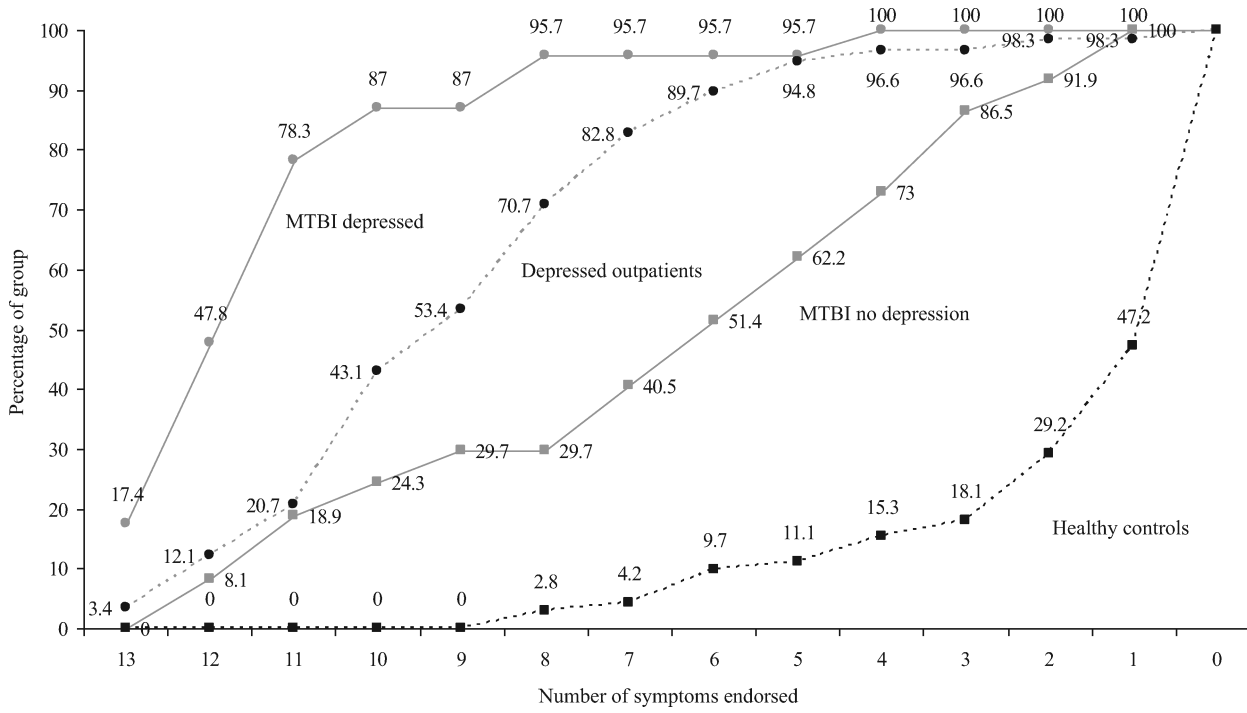
scores of 3 or more) in each group are presented in Table 2.* Overall, the MTBI-depressed group had the highest rates of symptom endorsement (mild and moderate), followed by the depressed outpatients, MTBI-no depression, and healthy control group.† For example, the range of specific endorsement rates of symptoms at a mild level or greater was as follows: MTBI-depressed group (65.2%–95.7%), depressed outpatient (34.5%–93.1%), MTBI-no depression (24.3%–70.3%), and healthy control (1.4%–23.6%).

The percentages of participants with BC-PSI total scores of 10 points or higher and 15 points or higher were calculated and compared. A score of 10 points or greater, and 15 points or greater, are considered to be "unusually high" and "extremely high," respectively, compared with those for healthy adults.[25] Chi-square analyses were used to compare the proportion of patients in each group whose BC-PSI total scores were classified into these 2 total score classification ranges. There were significant differences in the proportion of patients with total scores of 10 points or higher for all 6 group comparisons (all $P < .05$), with the exception of the comparison between MTBI-depressed and depressed outpatients (Fisher exact test: $P = .682$). The MTBI-depressed (95.7%) and depressed outpatient group (94.8%) had the highest proportion of patients with scores in this range, followed by the MTBI-no depression (62.2%) and healthy control group (8.3%). Similarly, for BC-PSI total scores of 15 points of higher, there were significant differences for all 6-group comparisons (all $P < .05$), with the exception of the comparison between the MTBI-depressed and depressed outpatient group (Fisher exact test: $P = .169$; it is notable, however, that there was a difference of 12% between these 2 groups). The MTBI-depressed (91.3%) group had the highest proportion of patients with scores in this range, followed by the depressed outpatient (79.3%), MTBI-no depression (40.5%), and healthy control group (4.2%).

Further comparison of the prevalence of endorsed symptoms was undertaken by considering all symptoms simultaneously. The cumulative percentages of the number of "mild or greater" symptom ratings for each group are presented in Figure 2. Chi-square analysis was used to compare the cumulative percentages of patients who endorsed "x-or-more" symptoms (ie, ranging from 1 to 13) across all 4 groups. Overall, the MTBI-depressed group endorsed the most symptoms, followed by depressed outpatients, patients with MTBI-no depression, and healthy controls.

For symptoms endorsed at a mild level or greater, the most notable differences were found at the middle to higher portion of the symptom endorsement curve. For

*These cutoff scores were used to be consistent with previous research using the BC-PSI and to maximize comparability between studies.
†Data for the 13 individual items have been included for descriptive purposes only. Formal statistical comparisons (χ^2 analyses) for the individual items were not undertaken because of the large number of comparisons required for 13 variables and 4 groups. Chi-square analysis results are reported only for the BC-PSI total scores.



BC-PSI, British Columbia Post-concussion Symptom Inventory.
Mild TBI not depressed ($n = 37$); Mild TBI depressed ($n = 23$); Healthy community controls, ($n = 72$); Depressed outpatients ($n = 58$); MTBI = mild traumatic brain injury.

Figure 2. Cumulative percentages of the number of symptoms endorsed on the BC-PSI by group: Mild or greater symptoms.

example, 95.7% of the MTBI-depressed group endorsed 8 or more symptoms at a mild level or greater, followed by 70.7% of the depressed outpatients, 29.7% of the MTBI-no depression group, and 2.8% of the healthy control group ($P < .05$ for all comparisons). Similarly, 87.0% of the MTBI-depressed group endorsed 10 or more symptoms at a mild level or greater, followed by 43.1% of depressed outpatients, 24.3% of MTBI-no depression, and 0% of the healthy control group ($P < .05$ for all comparisons).

The percentages of each group that met *ICD-10* Category C symptom criteria for postconcussional disorder were calculated. According to these criteria, a person must have at least 3 of the following 6 symptom categories: (1) headaches, dizziness, general malaise, excessive fatigue, or noise intolerance; (2) irritability, emotional lability, depression, or anxiety; (3) subjective complaints of concentration or memory difficulty; (4) insomnia; (5) reduced tolerance to alcohol; and (6) preoccupation with these symptoms and fear of permanent brain damage. Based on symptom reporting as mild or greater in 3 or more of the 6 symptom domains, the percentages of each group that met ICD-10 symptom criteria were as follows: MTBI-depression = 100%, depressed outpatients = 96.6%, MTBI-no depression = 83.8%, and healthy controls = 13.9%. Post hoc analyses (using chi-square analyses) revealed significant differences in the proportion of patients who met ICD-10 criteria for all 6-group comparisons (all $P < .05$), with the exception of the comparison between MTBI-depressed and depressed outpatients ($P = .367$).

The percentages of each group that met ICD-10 symptom criteria for postconcussional disorder, based on symptom reporting in each domain as *moderate or greater*, were as follows: MTBI-depression = 95.7%, depressed outpatients = 82.8%, MTBI-no depression = 48.6%, and healthy controls = 1.4%. Post hoc analyses again revealed significant differences in the proportion of patients who met ICD-10 criteria for all 6-group comparisons (all $P < .001$), with the exception of the comparison between MTBI-depressed and depressed outpatients ($P = .127$).

DISCUSSION

The purpose of this study was to examine the influence of depression on postconcussion symptom reporting in a cohort of patients following MTBI. We compared MTBI patients with and without depression with depressed outpatients and healthy controls. MTBI patients were carefully classified into depressed/not-depressed subgroups on the basis of hallmark symptoms of depression that were least likely to overlap with postconcussion symptoms. It was hypothesized that patients with depression

following an MTBI would report symptoms similar to uninjured outpatients with depression, and that both of these groups would endorse more symptoms than patients with MTBIs who were not depressed and healthy control subjects.

There were 4 specific hypotheses for this study. The results strongly supported the first 3 hypotheses, but not the fourth. Consistent with the first 2 hypotheses, (i) MTBI patients with and without depression reported more postconcussion symptoms than healthy controls and (ii) MTBI patients with depression reported more postconcussion symptoms than MTBI patients without depression. Consistent with the third hypothesis, depressed outpatients reported more symptoms than both healthy controls and MTBI patients without depression. The final hypothesis was that the symptom reporting between MTBI patients with depression and uninjured outpatients with depression would be comparable. There were mixed findings relating to this hypothesis. Compared to the outpatients with depression, the MTBI patients with depression (i) had greater total scores on the BC-PSI, (ii) had a greater percentage of individuals who endorsed some individual symptoms, and (iii) had an overall greater number of endorsed symptoms. However, in contrast, there was no difference in the proportion of patients who (i) met ICD-10 symptom criteria for postconcussional disorder for symptom domains endorsed as mild or greater or moderate or greater, or (ii) had BC-PSI total scores that were 10 points or more or 15 points or more.

Although the impact of MTBI alone on postconcussion symptom reporting was very large (Cohen $d = 2.05$), there was an obvious greater impact on postconcussion symptom reporting when a depressive experience accompanied MTBI (Cohen $d = 5.41$). These results are consistent with studies that have established depression as having a significant impact on postconcussion symptom reporting following MTBI.[7,58] The large "additive effect" of depression on postconcussion symptom reporting following MTBI was somewhat surprising. There was a very large effect size between the MTBI-no depression and MTBI-depressed groups. In clinical terms, the vast majority (95.7%) of the MTBI-depressed group met ICD-10 symptom criteria for postconcussional disorder (based on symptom reporting in each domain as moderate or greater) compared to fewer than half (48.6%) of the MTBI-no depression group. These differences are striking.

In the absence of an MTBI, depression alone had an enormous impact on postconcussion symptom reporting when compared to nondepressed healthy controls. In addition, depression alone had a greater impact on postconcussion symptom reporting than MTBI alone. The vast majority of the depressed outpatient group (96.6%) met ICD-10 symptom criteria for postconcussional disorder based on symptom reporting in each domain as mild or greater, and a substantial majority (82.8%) also met ICD-10 symptom criteria based on symptom reporting as moderate or greater. When taken as a whole, these findings suggest that depression appears to have an obvious and greater impact on symptom reporting compared to MTBI alone, but depression occurring comorbidly with MTBI is associated with an extremely high symptom burden.

Clearly, what are commonly considered to be postconcussion symptoms were extremely common in this sample of depressed outpatients. This is consistent with previous studies that have reported at least moderate correlations between postconcussion symptoms and depression[59] or life stress.[60–65] Patients with MTBIs complicated by a depressive experience endorsed an extremely high number of symptoms. When compared to healthy controls, the effect size was very large. When compared to depression alone, the effect size was large. When taken as a whole, these findings suggest that depression appears to have an obvious and greater impact on symptom reporting compared with MTBI alone, but depression occurring comorbidly with MTBI is associated with an extremely high symptom burden.

This study has several limitations. First, these findings should not be considered generalizable to all people who have sustained MTBIs. This is a highly selected, nonrepresentative, yet homogenous sample. Approximately 35% of the MTBI sample were excluded because they could not be classified into 1 of the 2 depression categories. As a group, these patients were reporting high levels of postconcussion symptoms (BC-PSI total score: $M = 27.9$, $SD = 9.3$). However, it was not possible to confidently differentiate the likely influence of depression versus MTBI on symptom reporting in these individuals. In order for us to attempt to isolate and examine the depressive experience, it was necessary to exclude a significant minority of patients.

Second, the MTBI-depression group was selected on the basis of symptoms whose etiology may not be solely attributable to depression alone and may also be attributable to the residual effects of MTBI. It is possible that some people in the MTBI-depression group are, in fact, not depressed but are experiencing symptoms related to the neurobiology of MTBI. It is impossible for us, or anyone else, to discern the precise etiology of these symptoms. However, we have made every effort to carefully select symptoms that were considered hallmark symptoms of depression that were least likely to overlap with postconcussion symptoms. Although it is not possible for us to say with certainty that all MTBI patients have been classified accurately in depressed/not-depressed groups, we believe that our selection method has minimized the potential impact of misclassification

as much as possible (within the limits of this research design).

Third, there was no measure of effort administered. The relation between effort test failure and elevated symptom reporting has been established for some time. Of particular relevance, Iverson and colleagues[55] have reported that failure on the test of memory malingering is associated with increased postconcussion symptom reporting following MTBI. It is possible that some of our patients exaggerated their symptoms. Although it is not possible to evaluate the influence of effort test failure here, it is possible to compare patients who are seeking/not seeking financial compensation for their injuries. There were no significant differences between litigants and nonlitigants in the TBI-depressed group ($d = 0.53$, medium effect size) or the TBI-no-depression group ($d = 0.37$, small effect size). However, there was a tendency for litigants to report more severe symptoms, but these analyses were underpowered because of small sample sizes. Overall, litigation status had, at most, a small effect on the results of this study. We could not, however, examine the issue of effort or exaggeration separately from litigation status.

In conclusion, these results suggest that the presence of depression, regardless of its etiology and course, will significantly increase self-reported PCS symptoms, in both the absence or presence of a past MTBI. These findings emphasize the necessity to consider depression as an important factor in the differential diagnostic process. The differential diagnosis of postconcussional disorder following MTBI is complicated by the presence of depression. The presence of depression in a person with a history of traumatic brain injury presents an obvious challenge if one attempts to diagnose a persistent postconcussion syndrome, given the overlap in symptoms. Certainly, depression is relatively common in patients with traumatic brain injuries,[33] although not necessarily more so than in patients with general trauma.[31,32] Depression is also common in persons with chronic pain,[66,67] and it is associated with increased disability in these patients. Therefore, patients seen long after an MTBI who have chronic pain, depression, or both are very likely to meet diagnostic criteria for a persistent postconcussion syndrome, even if the problems associated with the MTBI have long since resolved. This is particularly important in a forensic setting. When seeing a person long after an injury, the clinician or forensic examiner must decide whether the current reported symptoms are caused by a low probability factor (the biological consequences of a remote MTBI) or a high probability factor (the presence of current depression, chronic pain, or both). The clinician or forensic examiner who diagnoses persistent postconcussion syndrome in a patient with comorbid depression, chronic pain, or both might be criticized for coming to an erroneous conclusion without considerable evidence to support this diagnosis.

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