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Mild traumatic brain injury does not predict acute postconcussion syndrome

S Meares,¹ E A Shores,¹ A J Taylor,¹ J Batchelor,¹ R A Bryant,² I J Baguley,³
J Chapman,³ J Gurka,³ K Dawson,^{1,2} L Capon,¹ J E Marosszeky³

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¹ Department of Psychology, Macquarie University, Sydney, Australia; ² Department of Psychology, University of New South Wales, Sydney, Australia; ³ Department of Rehabilitation Medicine, Westmead Hospital, Sydney, Australia

Correspondence to:
E A Shores, Department of Psychology, Macquarie University, North Ryde, New South Wales, 2109, Australia; ashores@psy.mq.edu.au

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ABSTRACT

Background: The aetiology of postconcussion syndrome (PCS) following mild traumatic brain injury (mTBI) remains controversial. Identifying acute PCS (within the first 14 days after injury) may optimise initial recovery and rehabilitation, identify those at risk and increase understanding of PCS.

Objective: To examine predictors of acute outcome by investigating the relationship between preinjury psychiatric disorder, demographic factors, injury related characteristics, neuropsychological and psychological variables and acute PCS.

Methods: Prospective study of consecutive trauma admissions to a level 1 trauma hospital. The final sample comprised 90 patients with mTBI and 85 non-brain injured trauma controls. Individuals were administered a PCS checklist, and neuropsychological and psychological measures. Multiple imputation of missing data in multivariable logistic regression and bivariate logistic regressions were used to predict acute PCS at a mean of 4.90 days after injury.

Results: Diagnosis of acute PCS was not specific to mTBI (mTBI 43.3%; controls 43.5%). Pain was associated with acute PCS in mTBI. The strongest effect for acute PCS was a previous affective or anxiety disorder (OR 5.76, 95% CI 2.19 to 15.0). Females were 3.33 times more likely than males to have acute PCS (95% CI 1.20 to 9.21). The effect of acute post-traumatic stress and neuropsychological function on acute PCS was relatively small. Higher IQ was associated with acute PCS.

Conclusions: There is a high rate of acute PCS in both mTBI and non-brain injured trauma patients. PCS was not found to be specific to mTBI. The use of the term PCS may be misleading as it incorrectly suggests that the basis of PCS is a brain injury.

Trauma patients frequently report neurological (eg, headache, dizziness) and psychological (eg, fatigue, anxiety, irritability) symptoms following acute mild traumatic brain injury (mTBI).¹ Acute neuropsychological difficulties with attention, information processing and memory generally resolve within 1–3 months.^{2,3} Up to 64% of individuals, however, continue to report three or more symptoms at 3 months.⁴ These persistent symptoms are commonly described as the post-concussion syndrome (PCS).⁵ The aetiology of PCS remains controversial,⁶ partly because the symptoms are not specific to mTBI, being found in other clinical conditions and in the normal population.^{6,7}

The predictors that relate to the development of PCS after mTBI have not been adequately identified.² Most research has focused on the chronic phase of recovery, variably defined as 1–3 months

after injury. The lack of research on acute PCS (ie, within 14 days of injury) is problematic. Firstly, acute PCS may have an immediate impact on initial recovery and rehabilitation. Secondly, understanding the aetiology of acute PCS may increase understanding of the acute cognitive, psychological and injury related factors that contribute to persistent PCS.^{1,2} Thirdly, identifying factors that contribute to persistent PCS may assist identification of patients at risk of subsequent psychological disorder.^{8,9}

To date, research has yielded inconsistent evidence about acute neuropsychological differences between patients with mTBI with PCS symptoms and controls.^{3,10,11} Several studies have reported that patients with mTBI perform worse than controls on neuropsychological measures.¹⁰ Others have found few differences.^{11,12} In patients with mTBI, the presence of PCS does not appear to influence reaction time, information processing or memory.^{1,13,14} These differences may be attributed to methodological factors.¹⁵

The World Health Organization (WHO) reports that few studies have adequately assessed the contribution of preinjury characteristics and injury related factors such as psychological distress, pain and medication to the reporting of acute PCS symptoms.² Some research points to psychological factors influencing acute PCS.^{1,10,15} Depression, anxiety and acute post-traumatic stress reactions are greater in mTBI participants with PCS than those without.^{1,13} Individuals with preinjury psychiatric disorders may be a more vulnerable group.^{16,17} The few studies that have examined the effect of pain on acute outcome have found contradictory results.^{10,18}

The purpose of the present study was to examine predictors of acute PCS by investigating the relationship between preinjury psychiatric disorder, demographic factors, injury related characteristics, neuropsychological and psychological variables and acute PCS. This investigation represents the first large scale study of acute PCS in a consecutive sample of hospitalised mTBI and trauma control (TC) patients, with groups carefully matched for preinjury and injury characteristics. This study also explores the utility of the diagnosis of acute PCS in mTBI and trauma patients.

It was hypothesised that patients with mTBI would have a greater likelihood of acute PCS than TC patients. Preinjury and demographic characteristics such as gender, age and IQ were expected to predict (ie, female gender, low IQ and older age) acute PCS.^{3,19} Preinjury psychiatric disorder was

also hypothesised to be predictive of acute PCS in mTBI and TCs.²⁰ Poor neuropsychological performance was anticipated to increase the likelihood of acute PCS in mTBI participants. Acute post-traumatic stress was expected to predict acute PCS in both mTBI and TCs.¹⁻⁸ Finally, injury related pain was hypothesised to predict acute PCS in both groups.

METHODS

Participants

Consecutive trauma admissions to a level 1 trauma hospital in Sydney, Australia, were prospectively included in the study if they had suffered a traumatic injury. Inclusion criteria included: (1) hospital admission within 24 h of injury; (2) initial assessment was not greater than 14 days post-trauma; (3) age between 18 and 65 years; (4) an IQ no less than 70; (5) not being the subject of forensic investigation; (6) no evidence of pre-existing cognitive impairment; (7) sufficient English language comprehension to allow for valid test administration; (8) no psychosis; (9) no physical injury as a result of self-harm; (10) being medically able to participate (eg, physical injuries did not prevent standard test administration); (11) not being an interstate or overseas visitor (to allow availability for 3 month and 12 month follow-up) and (12) not pregnant to avoid possible pregnancy associated cognitive deficits.

Mild uncomplicated TBI was defined according to the WHO Collaborating Task Force on mTBI criteria,¹⁵ with the exception of including individuals who had sustained an intracranial lesion not requiring surgery. WHO criteria require an acute brain injury to result from mechanical energy to the head from external physical forces and (i) one or more of the following: confusion or disorientation, loss of consciousness for 30 min or less, post-traumatic amnesia (PTA) for less than 24 h and/or other transient neurological abnormalities such as focal signs or seizure; and (ii) a Glasgow Coma Scale (GCS) of 13–15 after 30 min or on presentation for healthcare.

Individuals who had a trauma related lesion present on cerebral CT scan were regarded as sustaining a moderate TBI and were excluded.¹⁹ A normal cerebral CT scan was reported in 76 (84.4%) of the mTBI participants. Cerebral CT scan was not performed in 14 (15.6%) individuals. All 14 presented with a GCS of 15, 11 with a PTA of less than 60 min and three of 61 min to 12 h.

The comparison group comprised non-brain injured patients hospitalised following traumatic injury who met the inclusion criteria described previously and did not meet criteria for

mTBI.¹⁵ For example, they did not report loss of consciousness or PTA.

Individuals with a prior mTBI, psychiatric history, medical history (eg, epilepsy, diabetes, hypertension, cardiac disease and other, such as hypothyroidism), marijuana or alcohol use were not excluded from either group. These factors were incorporated as they are known to influence outcome and to reduce the risk of confounding due to selection factors.³⁻¹⁵

The data were collected between April 2004 and June 2006. During this time, 4247 trauma admissions were screened and 342 met the inclusion criteria (fig 1). Consent was obtained from 227 (66.4%) participants; 115 (33.6%) refused consent. A total of 209 (61.1%) were assessed (18 participants being discharged prior to the assessment). A further 34 cases were excluded after assessment. Figure 1 presents a flow chart of those excluded. The final sample comprised 90 patients with mTBI and 85 TCs.

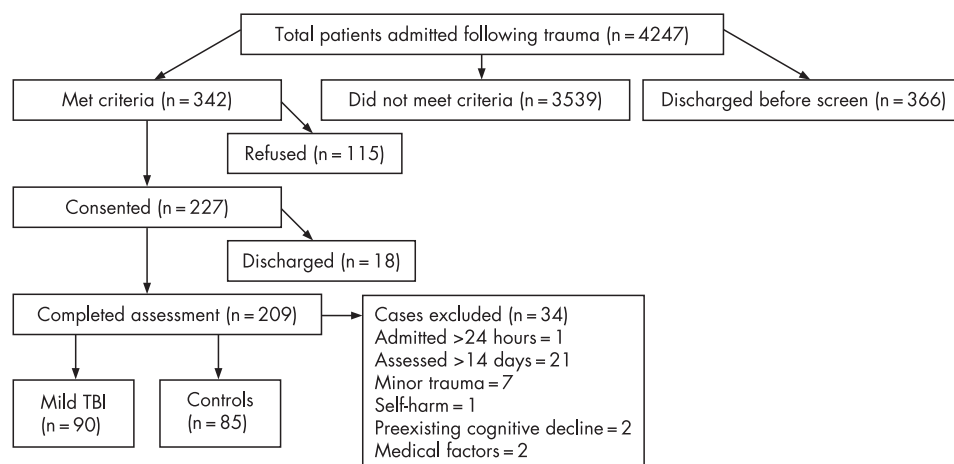
Individuals who refused to participate in the study did not differ from those who consented in terms of gender ($\chi^2 = 0.238$; $p = 0.626$), age ($t_{340} = 0.682$; $p = 0.496$), injury severity ($t_{340} = -0.519$; $p = 0.604$) or days hospitalised ($t_{340} = -0.550$; $p = 0.583$). Those who were discharged before being screened for suitability ($n = 366$) did not differ from those who consented in terms of gender ($\chi^2 = 2.65$; $p = 0.103$) or age ($t_{591} = 1.24$; $p = 0.215$) but they differed significantly in terms of injury severity ($t_{591} = 3.44$; $p = 0.001$) and length of hospital stay ($t_{591} = 6.50$; $p = 0.001$). These individuals had lower injury severity scores and were in hospital for fewer days.

Measures

Diagnosis of PCS

A diagnosis of acute PCS was made based on the presence and frequency of three or more PCS symptom complaints from the International Classification of Diseases (ICD-10),²¹ diagnostic criteria for PCS.¹⁻⁴ PCS symptoms were assessed using the Post Concussion Syndrome Checklist (PCSC); a valid PCS measure.²² The PCSC contains six of the seven (fatigue, dizziness, poor concentration, memory problems, headache and irritability) PCS symptoms from the ICD-10 diagnostic criteria that have been reported to differentiate between mTBI and control groups at 1 month postinjury.²³ The 10 item PCSC was modified by adding three PCS symptoms (malaise, mood swings—emotional lability and insomnia) to allow the checklist equivalence to symptoms described in ICD-10, PCS symptom criteria.²¹ Participants were asked to rate the frequency of postconcussion

Figure 1 Participants consecutively admitted following trauma from April 2004 to June 2006. TBI, traumatic brain injury.



symptoms since the accident, on the PCSC, using a five point rating scale (1 = "Not at all", 5 = "All the time"). A symptom was regarded as clinically significant when endorsed as 3 ("often") and above, and was characterised as a current PCS symptom.^{6 24}

Neuropsychological tests

Neuropsychological tests were selected on the basis of sensitivity to deficits in mTBI or as a measure of premorbid IQ. Consistent Longer Term Retrieval score (CLTR) is from the Westmead Selective Reminding Test, a 10 word, 10 trial measure of verbal new learning.²⁵ All patients were administered one or other of two alternate forms. Mann-Whitney U tests revealed there were no significant differences between the forms (mTBI, $z = -0.317$, $p = 0.75$; control, $z = -0.497$, $p = 0.62$) and therefore scores were combined.

Symbol-Digit Modalities Test, oral version (SDMT-oral), was used to measure auditory response speed.²⁶ The raw data were converted into age and education adjusted t scores.

Sequential Reaction Time (SEQRT1) subtest from the abbreviated California Computerised Assessment Package assessed for reaction time and information processing speed.²⁷

The Wechsler Test of Adult Reading and demographic variables were used to estimate pretrauma demographic predicted Wechsler Adult Intelligence Scale-III, Full Scale IQ scores.²⁸

Psychological measures

The Acute Stress Disorder Scale (ASDS) is a 19 item self-report inventory based on criteria from the Diagnostic and Statistical Manual of Mental Disorders (4th edition, DSM-IV) for acute stress disorder.^{29 30} The dissociative score (ASDS-DISS) from the dissociative cluster and a cumulative score from the sum of the re-experiencing, avoidance and arousal clusters (ASDS-Total) were analysed. Scores for the dissociative cluster were examined with the dissociative amnesia item and the numbing item excluded as research has suggested that these items directly overlap with amnesia associated with brain injury.⁹

The Mini-International Neuropsychiatric Inventory, V.5.0.0 (MINI), a structured diagnostic interview for DSM-IV and ICD-10 psychiatric disorders, was used to assess prior history of affective, anxiety and substance use disorders.³¹ MINI interviews were audiotaped and reviewed for quality control.

Alcohol Use Disorders Identification Test is a 10 item WHO questionnaire used to screen for current alcohol consumption (score range is from 0 to 40, with scores of 8 and above recommended as possible indicators of hazardous and harmful drinking).³²

Procedures

The study was approved by institutional ethics committees. Participants were identified through the daily trauma list. After obtaining informed consent, participants were assessed on demographic, preinjury factors and a larger battery of cognitive and psychological tests of which a subgroup was used for the present study.

Hospital records were used to obtain acute GCS and cerebral CT results. Mode of injury and daily opioid analgesia usage (from the day of trauma to the time of test administration) was documented. Opiate dosages were converted to oral morphine dose equivalents using an equianalgesic conversion calculator for acute dosing.³³ Tramadol dosages were also converted to oral morphine dose equivalents using recommended guidelines.³⁴

Duration of PTA was estimated retrospectively by asking participants "What is the first event you can remember after the injury?" and "What happened next?" until their description reflected detailed and continuous memories.³⁵ Ambulance records and hospital notes were reviewed to confirm the details of memories described by participants. No participant was in PTA at the time of assessment.³⁵

Injury Severity Score (ISS) ratings, based on the Abbreviated Injury Scale were made by Abbreviated Injury Scale certified research psychologists derived from hospital record review.³⁶ The ISS ratings did not include mTBI in the calculation of ISS scores.

Individuals were asked to estimate the severity of their pain, at the time of assessment, on a 11 point rating scale (0 = "no pain", 10 = "pain as bad as it could be").³⁷

RESULTS

Preinjury, demographic and injury related characteristics

Table 1 presents the mean patient characteristics and group comparisons for patients with mTBI and TCs. To control for multiple comparisons, an alpha level of 0.004 was set to provide an overall rejection level of 0.05. There were no significant group differences.

Effects of opioid analgesia on neuropsychological and psychological performance

On the day of assessment, 60.6% (mTBI, $n = 51$; TCs, $n = 55$) of the participants were administered opioid analgesia (table 1). Univariate analyses did not reveal an effect of opioids administered on the day of assessment on neuropsychological or psychological measures in either the mTBI or TC group.

Prevalence of preinjury psychiatric disorders

Table 2 presents the prevalence of preinjury psychiatric disorders for mTBI and TCs. The individual MINI diagnoses were grouped to form categories as shown in table 2. There were no significant differences between mTBI and TCs on these categories or on individual MINI diagnoses. Lifetime population prevalence of the individual DSM-IV disorders is shown for comparison.^{30 38}

PTA as a predictor of PCS

There was no significant difference ($\chi^2 = 0.671$; $p = 0.880$) in duration of PTA between individuals in the mTBI group who were diagnosed with PCS ($n = 39$) and those who were not ($n = 51$), based on χ^2 analysis.

Prediction model of PCS

Based on the previous results, mTBI and TCs were combined for further analyses, but were differentiated by a grouping variable. The dependent variable was the presence or absence of PCS in the combined groups.

The MINI was introduced into the study after data collection commenced; therefore, 13 individuals did not have MINI data. Two participants were discharged before administration and were unable to be contacted, and two others declined to complete the full MINI. Multiple imputation of missing data in multivariable logistic regression was performed.³⁹ Five samples containing imputed values were generated and the results of logistic regression analyses performed on each data set were combined.

Of the 175 participants, 76 (43.4%; 39 mTBI, 37 TCs) were diagnosed with PCS a mean of 4.90 (SD 2.63) days following

Table 1 Demographic, preinjury and injury characteristics of the participants

Variable	mTBI (n = 90)	Controls (n = 85)	p Value
Age at injury (y) (mean (SD))	34.7 (13.7)	34.6 (12.1)	0.780*
Years of education (mean (SD))	11.5 (2.8)	11.5 (2.5)	0.590
Full Scale IQ (mean (SD))	99.8 (10.4)	99.8 (9.8)	0.912
Assessed (days) (mean (SD))	4.8 (2.8)	5.0 (2.5)	0.310
AUDIT	6.6 (6.5)	5.2 (6.3)	0.015
Injury severity score (mean (SD))	5.4 (6.2)	5.5 (5.3)	0.329
Pain	3.6 (2.4)	3.9 (2.6)	0.635
	mTBI (n = 51)	Controls (n = 55)	
Opioids, MDE (mean (SD))	49.5 (87.6)	39.5 (38.1)	0.831
Sex (n (%))			
Males	61 (67.8)	55 (64.7)	
Females	29 (32.2)	30 (35.3)	0.667†
No of prior mTBI (n (%))			
None	53 (58.9)	64 (75.3)	
One	30 (33.3)	11 (12.9)	
More than one	7 (7.8)	10 (11.8)	0.006
Marijuana use			
No	67 (74.4)	68 (80.0)	
Yes	23 (25.6)	17 (20.0)	0.382
Medical history (n (%))			
No	72 (80.0)	66 (77.6)	
Yes	18 (20.0)	19 (22.4)	0.703
Cause of injury (n (%))			
Motor vehicle accident	73 (81.1)	63 (74.1)	
Fall/jump	10 (11.1)	16 (18.8)	
Assault	5 (5.6)	4 (4.7)	
Other	2 (2.2)	2 (2.4)	0.542‡
Glasgow Coma Scale (n (%))			
13	2 (2.2)		
14	11 (12.1)		
15	77 (85.7)		
Duration of PTA (n (%))			
<5 min	33 (36.7)		
6–60 min	20 (22.2)		
61 min to 12 h	21 (23.3)		
>12 h to 24 h	16 (17.8)		

Assessed (days), number of days assessed since trauma.

Medical history includes individuals with a history of epilepsy, diabetes, hypertension and cardiac disease.

Pain was measured on a numerical rating scale at the time of assessment.

AUDIT, Alcohol Use Disorders Identification Test; MDE, morphine dose equivalents; mTBI, mild traumatic brain injury, PTA, post-traumatic amnesia.

*Mann–Whitney U tests.

† χ^2 analyses.

‡Fisher's exact test.

trauma. Logistic regression was used to produce a prediction model of PCS with the following predictor variables: age, gender,^{3 19} Full Scale IQ, mTBI and TC grouping variable, CLTR, SDMT-oral, SEQRT1, ASDS-DISS,^{1 8} ASDS-Total,^{1 8 13} AXIS-I (at least one preinjury affective or anxiety disorder),^{17 20} SUBS (at least one preinjury substance use disorder)^{17 20} and pain.¹⁸ Interaction terms were entered to see whether the relationship between pain and acute PCS was different for mTBI and TCs. Significance was set at an alpha level of 0.05.

The fit of the model was examined through regression diagnostics. One case with very large residual values was subsequently deleted. Logistic regression was performed with 174 cases and the same results were obtained.

As presented in table 3, female gender, Full Scale IQ, SDMT-oral, ASDS-Total, AXIS-1 and pain were significant predictors of acute PCS, a mean of 4.90 days following trauma, after adjustment for all other variables. Examination of adjusted

effects indicated that the odds of acute PCS were greater for females than males. A higher IQ increased the likelihood of acute PCS. As SDMT-oral t scores increased (normalised), the possibility of a diagnosis of acute PCS reduced. Each unit increase in ASDS-SUM increased the odds of acute PCS. The strongest effect for acute PCS was at least one previous affective or anxiety disorder. With each unit increase in pain, the odds of acute PCS increased in patients with mTBI, whereas for TCs each unit increase in pain reduced the likelihood of acute PCS. The area under the receiver operating characteristic curve for the adjusted model was 0.887 indicating very good discrimination in predicting those with acute PCS and those without. The model was well calibrated (χ^2_8 ; $p = 0.477$).

The results of bivariate logistic regressions are also shown in table 3. In comparison with unadjusted Full Scale IQ and unadjusted SDMT-oral, adjusted Full Scale IQ and adjusted SDMT-oral each made a significant contribution to the

Table 2 Prevalence of preinjury psychiatric disorder in patients with mild traumatic brain injury and trauma controls admitted following trauma

	Population prevalence (%)	n	mTBI (n (%))	n	Controls (n (%))	p Value*
Affective disorders						
Major depression	16.6	77	19 (24.7)	83	15 (18.1)	0.308
Dysthymia	2.5	77	1 (1.3)	83	1 (1.2)	1.000‡
Any affective disorder†	–	77	20 (26.0)	83	16 (19.3)	0.311
Anxiety disorder						
Panic disorder	4.7	77	11 (14.3)	83	4 (4.8)	0.056‡
PDLS attacks	–	77	3 (3.9)	83	4 (4.8)	1.000‡
Agoraphobia	1.4	76	9 (11.8)	83	9 (10.8)	0.843
Social phobia	12.1	76	9 (11.8)	83	6 (7.2)	0.320
OCD	1.6	75	7 (9.3)	83	7 (8.4)	0.842
PTSD	6.8	76	17 (22.4)	83	12 (14.5)	0.197
GAD	5.7	77	9 (11.8)	83	12 (14.5)	0.627
Any anxiety disorder†	–	77	32 (41.6)	83	29 (34.9)	0.389
At least one disorder†	–	77	35 (45.5)	83	33 (39.8)	0.467
Substance use disorders						
Alcohol abuse	13.2	76	16 (21.1)	83	21 (25.3)	0.527
Alcohol dependence	5.4	76	10 (13.2)	83	12 (14.5)	0.813
Marijuana abuse	4.0	76	11 (14.5)	83	12 (14.5)	0.998
Marijuana dependence	4.0	76	8 (10.5)	83	9 (10.8)	0.948
Any substance use disorder†	–	76	20 (26.3)	83	24 (28.9)	0.714

Disorder, Affective, Anxiety and Substance use disorders were diagnosed using the Mini-International Neuropsychiatric Interview. Panic disorder includes those with/without agoraphobia, Agoraphobia is agoraphobia without panic disorder.

At least one diagnosis denotes the number of individuals who meet criteria for at least one preinjury affective or anxiety disorder.

Any substance use disorder denotes at least one preinjury substance disorder.

* χ^2 analyses.

†Individual MINI diagnoses were grouped to form each category.

‡Fisher's exact test.

GAD, general anxiety disorder; mTBI, mild traumatic brain injury; OCD, obsessive compulsive disorder; PDLS, panic disorder limited symptom; PTSD, post-traumatic stress disorder.

association of acute PCS. ASDS-DISS failed to make a significant contribution to prediction in the multivariable analysis although it was significant in the bivariate analysis.

This is likely to be due to the moderately strong correlation between ASDS-Total and ASDS-DISS (mTBI, $r = 0.511$; control, $r = 0.596$).

Table 3 Adjusted and unadjusted logistic regression models for predicting acute postconcussion syndrome

Predictor	Adjusted OR (95%CI)	p Value	Unadjusted OR (95% CI)	p Value
Age	0.98 (0.95–1.02)	0.277	0.99 (0.97–1.01)	0.328
Sex, Females	3.33 (1.20–9.21)	0.020*	3.41 (1.77–6.56)	<0.001**
Full Scale IQ	1.06 (1.01–1.11)	0.014*	1.00 (0.98–1.04)	0.610
mTBI/Control	0.73 (0.31–1.73)	0.475	0.97 (0.53–1.76)	0.912
CLTR	0.99 (0.98–1.02)	0.981	1.00 (0.99–1.02)	0.854
SDMT-oral	0.93 (0.88–0.98)	0.008*	0.97 (0.94–1.00)	0.063
SEQRT1	1.00 (0.99–1.00)	0.126	1.00 (0.99–1.00)	0.573
ASDS-DISS	1.06 (0.86–1.31)	0.576	1.29 (1.13–1.46)	<0.001**
ASDS-Total	1.07 (1.01–1.12)	0.013*	1.12 (1.07–1.16)	<0.001**
AXIS-1, present	5.76 (2.19–15.0)	<0.001**	5.26 (2.74–10.12)	<0.001**
SUBS, present	0.79 (0.28–2.25)	0.661	1.11 (0.57–2.15)	0.765
Pain	1.11 (0.90–1.38)	0.322	1.38 (1.20–1.60)	<0.001**
Pain*mTBI	1.57 (1.06–2.30)	0.022*		
[Pain*Control	0.64 (0.43–0.94)	0.022*]		

Sex was dummy coded with male as the reference category.

mTBI/Control, a grouping variable for mTBI and trauma control groups was dummy coded with control as the reference category. Pain was measured on a verbal numerical rating scale; Pain*mTBI, interaction term, with control dummy coded as the reference category; Pain*Control, interaction term, with mTBI coded as the reference category.

ASDS-DISS, the dissociative cluster score from the Acute Stress Disorder Scale without the dissociative amnesia and numbing items; ASDS-Total, sum of the re-experiencing, avoidance and arousal cluster scores from the Acute Stress Disorder Scale; AXIS-1, at least one preinjury affective or anxiety disorder (AXIS-1 was dummy coded as an absence of a preinjury anxiety or affective disorder as the reference category); CLTR, Continuous Longer Term Retrieval score from the Westmead Selective Reminding Test; mTBI, mild traumatic brain injury; SDMT-oral, Symbol Digit Modalities Test-oral version; SUBS, at least one preinjury substance use disorder (SUBS was dummy coded as an absence of a preinjury substance use disorder as the reference category); SEQRT1, Sequential Reaction Time 1 from the California Computerised Assessment Package.

* $p < 0.05$; ** $p < 0.001$.

DISCUSSION

In this study a previous affective or anxiety disorder, female gender, higher IQ, response speed, acute post-traumatic stress and pain were significant predictors of acute PCS.

Of 175 participants, 43% were diagnosed with acute PCS approximately 5 days postinjury (per ICD-10, PCS symptom complaints).²¹ Individuals met criteria if they reported three or more current symptoms,^{1,4} suggesting that acute PCS may be made up of divergent symptom patterns. The prediction model indicated that a diagnosis of acute PCS was not specific to mTBI participants (mTBI 43%; TCs 44%). The frequency of acute PCS in mTBI participants is similar to that previously reported by Meares *et al.*¹ Few other studies have examined the incidence of PCS using ICD-10 symptom complaints in the acute stage of recovery.

It could be argued that the non-specificity of acute PCS may be accounted for by TCs having sustained an occult brain injury.¹⁹ Medical details and interview data of each participant, however, were judiciously evaluated against the WHO mTBI criteria.¹⁵ None of the TCs reported amnesia.³⁵ High base rates of PCS have been reported in the normal population,^{6,7,23,24} non-brain injured trauma patients^{10,19} and in other clinical groups.⁶ These findings provide additional evidence that acute PCS is present in trauma inpatients and that acute PCS is not specific to mTBI.

The finding that females are three times more likely than males to have acute PCS is consistent with the literature.^{5,19} These sex differences may be due to acute psychobiological reactions which have been proposed to differ in females relative to males following acute stress.⁴⁰ Age has been found to be an inconsistent predictor of outcome and was not found to be associated with acute PCS.¹⁹ Higher intellectual capacity was more likely to be associated with increased acute PCS. This finding may only apply in the acute stage as Luis and colleagues²⁴ have reported that lower intellectual capacity is associated with persistent PCS.

Partial support for the hypothesis that neuropsychological function is related to acute PCS was found in the relationship between response speed and acute PCS. As response speed increased (normalised) in both groups, acute PCS reduced. There were no differences in neuropsychological test performance between mTBI and TCs, with and without acute PCS. Acute post-traumatic stress, due to whether or not the injury is trauma related (eg, motor vehicle accident, assault versus a fall), may impact on neuropsychological test performance and be related to persistent PCS symptoms.^{11,19} Both patients with mTBI and TCs experienced similar mechanisms of trauma related injury. A limitation of the current study was the absence of a normal comparison group which would allow the hypothesis regarding trauma effects to be tested.

Individuals after mTBI with increasing levels of pain were vulnerable to acute PCS, in comparison with similar TC participants. This interaction has not been reported previously. There was no difference between mTBI and TCs in ISS, opioid analgesia or pain recorded on the day of assessment. The results suggest a unique relationship where acute pain appears to moderate acute outcome in mTBI. It is not unreasonable to hypothesise that acute pain may have additional effects on brain function following mTBI that predispose to acute PCS.

Acute PCS was more likely with increasing levels of acute post-traumatic stress. Post-traumatic stress disorder (PTSD) has been noted to be comorbid with persistent PCS.¹⁹ More apparent symptoms have been described in mTBI individuals with PTSD than in those without PTSD.⁸ The current findings

suggest that the effect of acute post-traumatic stress on acute PCS is relatively small; however, acute PCS may influence the later development of PTSD through a more difficult post-trauma adjustment.⁸

Preinjury substance use disorder was not related to acute PCS. Substance use disorder diagnosis initially increases after traumatic injury.^{17,20} Accordingly, postinjury substance use disorder may be predictive of PCS in the chronic stage of recovery. A preinjury episode of at least one affective or anxiety disorder resulted in individuals being six times more likely to develop acute PCS. Similar results have been reported by Luis and colleagues²⁴ who found that males, with and without mTBI, with a history of internalising problems (anxiety, depression, mania and psychosis) in early adulthood were 3–4 times more likely to report persistent PCS. The present study extends these findings to the acute stage of recovery, to males and females, and to a trauma inpatient group.

A large number of patients with mTBI (67%) and TCs (60%) with acute PCS had a previous affective or anxiety disorder. There was largely no evidence of a difference in the type of PCS symptom endorsed (ie, neurological or psychological). The single difference was that a greater number of TCs with a previous affective or anxiety disorder reported anxiety in comparison with those without psychological histories (70% vs 30%). Of the TCs, only 24% (n = 20) reported anxiety as a current PCS symptom.

The prevalence of preinjury affective and anxiety disorder in participants was high.^{30,38} These individuals are at risk of subsequent psychiatric illness.^{17,20} Those with mTBI are also at risk of persistent psychiatric illness.¹⁷ The vulnerability of people with preinjury psychiatric disorder highlights the need to identify affected individuals because they may require specific intervention to manage distressing reactions in the acute phase.

In conclusion, these results identify a high rate of acute PCS, early in the recovery of trauma patients, irrespective of mTBI status. Because PCS is not specific to mTBI,² the use of ICD-10 diagnostic criteria for PCS is problematic and may be misleading as it incorrectly suggests that the basis of PCS is a brain injury.² Whereas pre-existing psychiatric disorder does appear important, neuropsychological factors do not appear to contribute greatly to acute PCS. The extent to which these factors also contribute to persistent PCS is central. Future studies need to carefully match mTBI and control patients on preinjury, demographic and injury related factors to determine the key predictors of persistent PCS. Efficient prediction of those at risk of PCS will facilitate better opportunities for early intervention and management.

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