Predictors of Postconcussive Symptoms 3 Months After Mild Traumatic Brain Injury

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Objective: There is continuing controversy regarding predictors of poor outcome following mild traumatic brain injury (mTBI). This study aimed to prospectively examine the influence of preinjury factors, injury-related factors, and postinjury factors on outcome following mTBI. Method: Participants were 123 patients with mTBI and 100 trauma patient controls recruited and assessed in the emergency department and followed up 1 week and 3 months postinjury. Outcome was measured in terms of reported postconcussional symptoms. Measures included the ImPACT Post-Concussional Symptom Scale and cognitive concussion battery, including Attention, Verbal and Visual memory, Processing Speed and Reaction Time modules, pre- and postinjury SF-36 and MINI Psychiatric status ratings, VAS Pain Inventory, Hospital Anxiety and Depression Scale, PTSD Checklist–Specific, and Revised Social Readjustment Scale. Results: Presence of mTBI predicted postconcussional symptoms 1 week postinjury, along with being female and premorbid psychiatric history, with elevated HADS anxiety a concurrent indicator. However, at 3 months, preinjury physical or psychiatric problems but not mTBI most strongly predicted continuing symptoms, with concurrent indicators including HADS anxiety, PTSD symptoms, other life stressors and pain. HADS anxiety and age predicted 3-month PCS in the mTBI group, whereas PTSD symptoms and other life stressors were most significant for the controls. Cognitive measures were not predictive of PCS at 1 week or 3 months. Conclusions: Given the evident influence of both premorbid and concurrent psychiatric problems, especially anxiety, on postinjury symptoms, managing the anxiety response in vulnerable individuals with mTBI may be important to minimize ongoing sequelae.

Keywords: traumatic brain injury, concussion, outcome assessment

Mild traumatic brain injury (mTBI) is a prevalent neurological condition, affecting 100–300 out of 100,000 annually (Cassidy et al., 2004; Hirtz et al., 2007). Although studies have shown that most cases make a full recovery within 3 months of injury, approximately 15%–25% of cases experience ongoing symptoms, which may cause significant disability (Carroll et al., 2004; Ponsford et al., 2000), with frequencies varying according to population studied, setting, and timing of recruitment (Belanger, Curtiss, Demery, Lebowitz, & Vanderploeg, 2005). The term postconcussion syndrome (PCS) refers to the somatic, cognitive, emotional, motor, or sensory symptoms ascribed to a concussion or head injury (Benton, 1989). These symptoms commonly include head-
aches, dizziness, visual disturbance, memory difficulties, poor concentration, mental slowness, difficulty dividing attention, alcohol intolerance, fatigue, irritability, depression, and anxiety (Carroll et al., 2004; Kraus et al., 2005; Lundin, de Boussard, Edman, & Borg, 2006; Ponsford et al., 2000; Yang, Tu, Hua, & Huang, 2007). Given the high frequency of mTBI, it is neither realistic nor necessary to provide comprehensive treatment to all people with these injuries. However, single-session therapies applied to at-risk individuals with mTBI may be efficacious (Mittenberg, Canyock, Condit, & Patton, 2001). Currently, clinicians assessing these patients do not have clear guidelines as to how to predict who is likely to experience ongoing symptoms. The early identification of such cases might allow for the early provision of management strategies to circumvent ongoing problems. Understanding the causes of ongoing PCS may also guide treatment.

Although numerous injury-related factors have been associated with continuing symptoms following mTBI, findings have been inconsistent (Carroll et al., 2004). The strongest predictors of outcome in moderate to severe TBI—namely, duration of loss of consciousness, initial Glasgow Coma Scores (GCS), and duration of posttraumatic amnesia (PTA), which are measures of injury severity—have not been shown to be significant predictors of ongoing sequelae following mTBI (Carroll et al., 2004; Ponsford et al., 2000). The reasons for this are unclear, but measurement issues may contribute to this (Ponsford et al., 2004). Although presence of intracranial abnormalities has been associated with poorer cognitive performance or persistent PCS in some studies (Lange, Iverson, & Franzen, 2009; Lewine et al., 2007; Lo, Shiftet, Gold, Bello, & Lipton, 2009; Sadowski-Cron et al., 2006; Williams, Levin, & Eisenberg, 1990), patients with uncomplicated mTBI do not show intracranial abnormalities. Poorer performances on cognitive tests of reaction time (RT), processing speed, immediate memory, verbal memory, and visual memory have also been documented in mTBI patients in relation to trauma controls early after injury (Landre, Poppe, Davis, Schmaus, & Hobbs, 2006; Peterson, Stull, Collins, & Wang, 2009; Ponsford et al., 2000; Sheedy, Geffen, Donnelly, & Faux, 2006; Shores et al., 2008), although there have been mixed findings regarding the relationship of cognitive impairments with PCS (Landre et al., 2006; Meares et al., 2008; Ponsford et al., 2000).

Of possible demographic predictors, female gender has been associated with greater reporting of PCS (Dischinger, Ryb, Kufera, & Auman, 2009; Meares et al., 2008; Ponsford et al., 2000). Age over 40 years was a negative prognostic factor in one study (Thornhill et al., 2000), but not other studies of mTBI, despite being a strong predictor of poorer outcome following moderate to severe TBI (Hukkelhoven et al., 2003). One study (Stulemeijer, Vos, Bleijenberg, & van der Werf, 2007) found that lower education predicted cognitive complaints 6 months postinjury. Findings regarding the effects of multiple concussive head injuries have been mixed. Results of a recent meta-analysis suggested that multiple self-reported concussions were associated with poorer performances on tests of delayed memory and executive function (Belanger, Spiegel, & Vanderploeg, 2010). However, the clinical significance of these differences was unclear.

The presence of preinjury psychiatric or other health problems and other life stressors have emerged as significant predictors of poorer mTBI outcomes in several studies (Carroll et al., 2004; Kashluba, Paniak, & Casey, 2008; McLean et al., 2009; Meares et al., 2008; Ruff, 2005; Wood, 2004). Concurrent anxiety, depression, and posttraumatic stress may contribute to symptoms (Bryant, 2008; Hoge et al., 2008; Stulemeijer et al., 2007), as may other injuries, pain, and medications (Carroll et al., 2004; Meares et al., 2006, 2008; Ponsford, 2005). Meares et al. (2006, 2008) found that a diagnosis of PCS an average of 4.9 days postinjury was just as likely in trauma controls as it was in patients with mTBI, in patients admitted to hospital with major trauma, with PCS predicted by previous affective or anxiety disorder, female gender, IQ, processing speed, and acute posttraumatic stress symptoms, but not presence of mTBI. Meares and colleagues (2008) raised doubts as to whether mild TBI contributes anything to symptoms over and above these factors. However, it is possible that the effects of anesthesia and analgesia impacted on findings in this group.

Increased reporting of symptoms may be associated with litigation or compensation-seeking (Binder & Rohling, 1996; Kashluba et al., 2008; Paniak et al., 2002). This will in turn depend upon the cause of injury and context of assessment. In a study focusing on mTBI cases with disappointing recoveries mostly in a litigation or compensation context, the variables most strongly related to outcome were depression, pain, and symptom invalidity on measures of response bias (Mooney, Speed, & Sheppard, 2005).

Thus it appears that mTBI is a complex condition. Potential contributing factors relate to preinjury factors (demographic variables including gender, age, and education; preinjury physical and psychiatric status; and history of previous head injury), injury-related factors (presence and severity of mTBI in terms of PTA duration and GCS, associated cognitive impairments), and the postinjury coexistence of pain, posttraumatic stress disorder (PTSD), other forms of anxiety, depression, other life stressors, and litigation. However, no study has prospectively examined the relative influence of all these factors in patients with uncomplicated mTBI and a general trauma sample recruited in the emergency department (ED) soon after injury not requiring general anesthesia. Therefore, the aim of this study was to prospectively examine the influence of the above-mentioned factors on outcome measured in terms of PCS 1 week and 3 months postinjury. It was hypothesized, on the basis of previous studies, that injury-related factors, including presence and severity of a mTBI, would have the strongest influence on outcome measured in terms of postconcussive symptoms at 1 week postinjury and that ongoing problems at 3 months postinjury would be predicted by a combination of mTBI presence and severity; psychological factors including anxiety, depression, pain, and PTSD; and other life stressors. It was considered important for clinicians to be able to predict, on the basis of factors known in the ED (i.e., preinjury and injury-related factors), what the outcome would be at both 1 week and 3 months postinjury. It was also considered important to be able to identify, on the basis of status at 1 week postinjury, when patients may be reviewed clinically, what factors predicted ongoing PCS at 3 months postinjury. Concurrent predictors were examined at each time point to identify causative factors relating to PCS at each time point.

**Method**

The study was conducted as part of a study examining outcome and the use of a revised version of the Westmead PTA Scale as a screening tool in patients with mTBI. It was approved by the
Alfred Hospital and Monash University Research Ethics Committees.

Participants

Participants were recruited consecutively from the Alfred Emergency & Trauma Centre (E&TC) in Melbourne, Australia. Inclusion criteria for the mTBI group included (1) recent (<24 hr) history of trauma to the head, resulting in loss of consciousness (LOC) <30 minutes, PTA <24 hours, and a GCS score of 13–15 on presentation to the ED; (2) age 18 years or over; and (3) English speaking. Participants were excluded if they (1) were intubated or required general anesthesia following injury; (2) had a breath alcohol reading >.05 at time of recruitment; (3) were under the influence of illicit substances at the time of injury; (4) had focal neurological signs, seizures, or intracerebral abnormality on computed tomography (CT); (5) had a dominant upper-limb injury that precluded use of a computer mouse; (6) were under spinal precautions and not to sit upright; (7) had a history of previous cognitive impairment, neurological illness, significant alcohol or drug abuse or other psychiatric impairment currently affecting daily functioning; or (8) were unavailable for follow-up. The trauma control (TC) group comprised patients presenting with minor injuries not involving the head and no LOC or PTA following their injury. Other inclusion and exclusion criteria were the same as for the mTBI group. Individuals with a medical history of nonneurological illness (e.g., cardiac disease, hypertension, cancer, diabetes), psychiatric history (excluding psychosis), prior mTBI, and reported alcohol or cannabis use were included in the study if they did not report any significant preinjury cognitive difficulties.

Measures

The dependent variable, PCS, was measured using the ImPACT Post-Concussion Symptom Inventory (Lovell & Collins, 1998) comprising 22 common concussion symptoms (e.g., headache, dizziness) with the severity ranging from 0 = none to 6 = severe. The list is more expansive than the criteria included in ICD-10. The symptoms were added into a total Post-Concussive Symptoms summary score, reflecting the number and severity of symptoms.

The following measures were examined as potential predictors of PCS:

**Preinjury factors.** Preinjury factors included age in years, gender, education in years, and previous head injury (yes/no; number of previous head injuries). Preinjury physical and mental health was assessed with the SF-36 Health Survey (SF-36; Jenkinson, Coulter, & Wright, 1993; Ware & Sherbourne, 1992), comprising a 36-item questionnaire, yielding an 8-scale health profile and two summary measures—a Physical Component Score and a Mental Component Score. Preinjury psychiatric history was assessed with the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998), a brief, reliable and valid structured diagnostic interview comprising 130 questions, screening for 16 Axis I Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM–IV) disorders and 1 personality disorder. Presence or absence of a diagnosis in each category was documented.

**Injury-related factors.** The Glasgow Coma Scale score (Teasdale & Jennett, 1976) utilizes the injured person’s best eye-opening, verbal, and motor responses to assess the conscious state, with a total score between 3 (showing no response) and 15 (alert and well oriented).

The PTA duration in days was determined by asking the patient what his or her first memory was after the injury and what had happened after that, until the patient could provide detailed and continuous recall of events after the injury. This was verified by examination of ambulance and hospital admission notes and discussion with accompanying persons. Patients were also screened using the revised Westmead PTA Scale (Ponsford et al., 2000), and if still in PTA on admission to the ED also had their orientation and ability to lay down new memories assessed prospectively at hourly intervals using this measure.

Cognitive performance was determined with the ImPACT concussive battery (Iverson, Lovell, & Collins, 2005), a computer-administered neuropsychological test battery consisting of five test modules, testing attention, verbal and visual memory, processing speed, and RT. Summary scores for each module were used in analyses.

**Postinjury factors.**

**Pain.** The Visual Analogue Scale (VAS) is a brief scale ranging from 0 (no pain) to 10 (extreme pain) used to measure pain. The VAS has been commonly used as a brief and convenient measure of pain for more than 30 years (Huskisson, 1974).

**Use of narcotic analgesia.** Yes/No

**Posttraumatic stress symptoms.** The PTSD Checklist—Specific (PCLS) is a self-report rating scale for assessing the 17 DSM–IV symptoms of PTSD on a 5-point scale from not at all to extremely. A total symptom severity score (range 17–85) is obtained by summing scores from the 17 items. The scale has been comprehensively validated (Blanchard, Jones-Alexander, Buckley, & Forneris, 1996; Forbes, Creamer, & Biddle, 2001).

**Anxiety and Depression.** The Hospital Anxiety and Depression Scale (HADS) is a validated self-assessment scale of current anxiety and depression symptoms, with 14 questions graded on a 4-point Likert scale (0–3), yielding separate anxiety and depression subscale scores of 0–21. The scale minimizes use of physical symptoms of mood disorders, which may be present in the medically ill (Snath & Zigmond, 1986). The validity and reliability of the HADS has been established in patients with TBI (Schönberger & Ponsford, 2010; Whelan-Goodinson, Ponsford, & Schönberger, 2009).

**Other life stressors.** The Revised Social Readjustment Rating Scale (RSRRS) measures 43 stressful events that happened in the last 12 months (Holmes & Rahe, 1967; Horowitz, Schaefer, Hirotu, Wilner, & Levin, 1977). The total score was recorded. These scores are interpreted as follows: low stress <149; mild stress = 150–200; moderate stress = 200–299; major stress >300.

**Litigation (yes/no).** Participants were asked to indicate whether (1) they were seeking compensation, (2) claims or charges had been made against them, and (3) any litigation had been resolved.

**Procedure**

Potential mTBI and TC participants were identified on the computerized E&TC patient list. Patients with mTBI were recruited after they had emerged from PTA, as assessed using the revised Westmead PTA Scale. After providing informed consent
and demographic information, participants completed the acute assessment at the hospital prior to discharge or, in a few cases, at home, but within 48 hours of injury. The acute assessment comprised a computerized concussion assessment battery (ImPACT) that also included the PCS to document current symptoms. The SF-36 was completed because it pertained to their general health and wellbeing prior to injury. This assessment took 45 min.

At 1 week follow-up, participants in both mTBI and TC groups completed the ImPACT cognitive battery, PCS measure, SF-36, HADS, and VAS as they pertained to current functioning. Information regarding current capacity for work, study, and functional activities was also collected. The MINI diagnostic interview was completed with respect to prevalence of lifetime preinjury psychiatric disorders. At the 3-month follow-up, participants repeated the same assessments. However, the SF-36 examined the participants’ general health over the preceding 4-week period, and the MINI examined psychiatric status within the 3 months since injury. Participants also completed the PCL-S to assess postinjury PTSD symptoms and the RSRRS to measure concurrent life stressors and reported on current employment status. These assessments took 1 hr.

### Analysis

Data analysis was undertaken with SPSS17 (SPSS, Inc., Chicago, IL), and statistical significance was reported at the 0.05 level. Missing values, of which there were very few, were excluded from descriptive statistics. Categorical variables were presented as percentages and continuous variables as medians and ranges. The main outcome was PCS. Preliminary correlational analyses were conducted using Spearman’s rho to examine both the correlations between the variables and PCS and the intercorrelations of the variables, because only a limited number of variables could be included in each model, and there was a need to avoid multicollinearity. Following these analyses, a series of generalized linear models (GLM) were computed to identify predictors of postconcussive symptoms at 1 week and 3 months postinjury. Because GLMs do not exclude cases with missing values, the only variables excluded were those that contributed to multicollinearity. Because the PCS scores were skewed, for use in regression analysis, PCS scores were grouped into three categories with equal frequencies. Because the PCS scores declined over time, the grouping was done separately for PCS scores at 1 week and 3 months as follows: The baseline PCS scores were divided into $\leq 16$, 17–35, and $\geq 36$. The PCS scores at 1 week were split into $\leq 5$, 6–23, and $\geq 24$. The PCS scores at 3 months were divided into 0, 1–8, and $\geq 9$. GLM is a flexible approach to multiple functions in the GLMs.

The GLMs were conducted in three models. Table 1 shows the predictors that were used in each model. The first model used information from time of injury to predict outcome, first at 1 week postinjury and separately at 3 months postinjury. The SF-36 Mental Health scale was removed to avoid collinearity with preinjury psychiatric status. The second model examined prediction of PCS, first at 1 week and second at 3 months postinjury on the basis of information known at 1 week postinjury. SF-36 Mental quality of life and HADS depression were removed from the model to avoid collinearity with other variables. Narcotics/analgesics were adjusted for only in the PCS 1-week model, because a significant number of participants were still using these. The third model examined the influence of both preinjury demographic and health factors and concurrent factors relating to cognitive function, pain, PTSD symptoms, general anxiety symptoms, and other life stressors on reported PCS at 3 months postinjury. The model was conducted to predict PCS at 3 months only. In order to examine whether the variables predicting outcome differed between mTBI and TC groups, models predicting 3-month PCS were conducted for mTBI and TC groups separately, using the same variables as in the previous models. The relationship between the presence of preinjury psychiatric disorders and HADS scores 1 week and 3 months postinjury was examined with Student t test. Group differences and changes over time in PCS and HADS were calculated with Mann–Whitney test, Wilcoxon signed-ranks test, and Friedman test because the variables were not normally distributed.

### Results

Participants were recruited between January 2007 and January 2009. During this period, 882 potential mTBI participants were admitted to the E&TC while it was staffed by a mTBI researcher, including evenings and weekends. Of these, 196 were eligible, and 123 were recruited into the study. Of 1404 potential TC participants, 338 were eligible and 100 were recruited and completed the acute assessment. The participant profiles are described in Table 2. Patients were predominantly young single men injured in motor

<table>
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<tr>
<th>Variable</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
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<tr>
<td>Preinjury</td>
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<tr>
<td>Gender</td>
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<td>✓</td>
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<tr>
<td>Age</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Psychiatric history (MINI)</td>
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<td>✓</td>
<td>✓</td>
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<tr>
<td>Physical health (SF-36)</td>
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<tr>
<td>Acute</td>
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<td>PTA duration</td>
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<tr>
<td>Visual memory (ImPACT)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Group (mTBI/control)</td>
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<td>✓</td>
<td>✓</td>
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<tr>
<td>1 week</td>
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<tr>
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<td>Visual memory (ImPACT)</td>
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<td>Pain (VAS)</td>
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<tr>
<td>Physical health (SF-36)</td>
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<td>Anxiety (HADS)</td>
<td>✓</td>
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<tr>
<td>Narcotic/analgesics</td>
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<td>3 months</td>
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<tr>
<td>Verbal memory (ImPACT)</td>
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<td>Visual memory (ImPACT)</td>
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<tr>
<td>Pain (VAS)</td>
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<td>PTSD symptoms (PCLS)</td>
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<tr>
<td>Stressful life events (RSRRS)</td>
<td>✓</td>
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</table>

Note. GLM = generalized linear models; MINI = Mini-International Neuropsychiatric Interview; SF-36 = Short-Form 36; PTA = posttraumatic amnesia; mTBI = mild traumatic brain injury; VAS = Visual Analogue Scale; HADS = Hospital Anxiety and Depression Scale; PTSD = posttraumatic stress disorder; PCLS = PTSD Checklist—Specific; RSRRS = Revised Social Readjustment Rating Scale. Developed to predict PCS at 1 week and 3 months. Developed to predict PCS at 3 months. Adjusted for only in the PCS at 1-week model.
vehicle collisions. There were no significant group differences in terms of gender, age, education, marital status, or employment status, or in history of previous mTBI. The mTBI group more commonly sustained assault-related injuries than did controls. More mTBI participants than controls had soft tissue injuries/lacerations.

At acute ED assessment, 77 (62.6%) TBI and 44 (44%) controls reported taking narcotic analgesics ($p = .006$). At 1 week, these numbers dropped to 20 (18.2%) in the TBI group and 19 (21.1%) in controls without any statistical group difference ($p = .603$). At 3 months the use of narcotic analgesics dropped to 2 patients in each group ($p = .905$).

Of the 120 mTBI participants with a known LOC status, 111 (92.5%) had a loss of consciousness (LOC) with the median LOC being 7 s, a mean of 61.44 ($SD = 110$) s, and a range of 0–10 min. Overall, 118 (96.7%) TBI participants had a reported period of PTA, with the median PTA being 15 min, a mean of 103 ($SD = 191$) min, and the range being 0–24 hr.

Of the 123 mTBI participants, 111 (90.24%) completed the 1-week assessment, and 90 (73.17%) completed the 3-month follow-up. Of the 100 TCs, 90 (90%) completed the 1-week follow-up and 80 (80%) the 3-month follow-up. There was no significant difference in gender between participants who consented to participate in the study and those who declined ($p = .369$). However, those who consented to participate were significantly older, with a median age of 32 years in comparison with 29 years for decliners ($p = .008$). The subsequent results are presented for those participants completing the 3-month follow-up only. The scores for PCS and HADS at each time point at which they were assessed are set out in Table 3. The groups differed significantly in terms of reported PCS, both on acute assessment in the ED and 1-week postinjury, with the mTBI group having more than double the Post-Concussive Symptom Inventory score of the control group at both time points. There was a significant decline in PCS over time. There were no significant differences in overall reporting of PCS at 3 months postinjury, nor did any particular symptom differentiate the groups. Applying the ICD-10 criteria used by Meares et al. (2008), 45.5% of mTBI participants and 14.0% of TCs reported a score of 4 or more on three or more of the ICD-10 symptoms at acute assessment in the ED ($p < .001$). However, neither these criteria nor any other cut-off score for PCS significantly differentiated the mTBI and TC groups at 1 week or 3 months postinjury. Groups did not differ on the HADS at acute assessment, 1 week, or 3 months postinjury. There was a significant reduction in anxiety and depression symptoms in both groups over time. More detailed results obtained by the mTBI and TC

<table>
<thead>
<tr>
<th>Table 2</th>
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<tr>
<td>Profile of Patients by Group</td>
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<tr>
<td>Demographics</td>
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<tr>
<td>Age (years)$^a$</td>
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<td>Education (years)$^a$</td>
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<td>Gender (male)$^b$</td>
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<tr>
<td>Married/de facto$^b$</td>
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<td>Employment status$^b$</td>
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<td>Full time</td>
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<td>Part time</td>
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<td>Casual</td>
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<td>Student</td>
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<tr>
<td>Not working</td>
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<tr>
<td>Cause of injury$^b$</td>
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<tr>
<td>Assault</td>
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<tr>
<td>Motor vehicle collision$^c$</td>
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<td>Bicycle collision</td>
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<tr>
<td>Fall</td>
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<tr>
<td>Sport injury</td>
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<tr>
<td>Other</td>
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<tr>
<td>Type of injury$^b$</td>
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<tr>
<td>Soft tissue/laceration</td>
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<tr>
<td>Fracture</td>
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<tr>
<td>Ligamentous</td>
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<tr>
<td>Dislocation</td>
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<tr>
<td>Involved in litigation$^b$</td>
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<tr>
<td>History of head injury$^b$</td>
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</tbody>
</table>

Note. Chi-square tests. TC = trauma control; mTBI = mild traumatic brain injury.
$a$ Values are given as median (range). $^b$ Values are given as N (percent-age). $^c$ This category includes motor vehicle, motorcycle, and pedestrian hit by vehicle collisions.
$p = .001$. $^{**} p < .001$.

<table>
<thead>
<tr>
<th>Table 3</th>
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<tr>
<td>Postconcussive Symptom (PCS) Scores and HADS Scores by Group at Each Time Point</td>
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<tr>
<td>Measure</td>
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<td>PCS total</td>
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<td>HADS Anxiety</td>
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<td>HADS Depression</td>
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Note. Probability values for the group comparisons are presented in the last column, and within-subject comparison results are provided in superscript below the tables. HADS = Hospital Anxiety and Depression Scale; TC = trauma control; mTBI = mild traumatic brain injury.
$a$ Median is given as minimum–maximum. $^b p < .001$ Friedman test showing decline in PCS over time in mTBI patients. $^c p < .001$ Friedman test showing decline in PCS over time in controls. $^d p = .002$ Wilcoxon signed-rank test showing a drop in HADS Anxiety over time in mTBI patients. $^e p < .001$ Wilcoxon signed-rank test showing a drop in HADS Anxiety over time in controls. $^f p < .001$ Wilcoxon signed-rank test showing decline in HADS Depression over time in mTBI patients. $^g p < .001$ Wilcoxon signed-rank test showing decline in HADS Depression over time in mTBI patients.
participants on each of the variables are detailed in another article (Ponsford, Cameron, Fitzgerald, Grant, & Mikocka-Walus, 2011).

**Predictors of Postconcussive Symptoms**

Preliminary correlational analyses revealed no significant association between education and PCS at 1 week (r = −.036, p = .618) or 3 months postinjury (r = −.074, p = .345). History of previous head injury was not significantly associated with PCS at 1 week (r = .052, p = .469) or 3 months postinjury (r = −.048, p = .540). Nor was there a significant association between seeking compensation/litigation and reported PCS at 3 months postinjury (r = .081, p = .298), with few participants seeking compensation. These variables were therefore not included in the predictive models.

Regarding the cognitive variables, as described by Ponsford et al. (2011), the mTBI participants differed significantly from TCs in performance on the ImPACT Visual Memory index only, whereas the group difference on Verbal Memory approached significance. There were no group differences apparent on the other scales. Moreover, these two variables showed the strongest correlations with PCS of each of the ImPACT summary scores (1-week Verbal Memory composite with 3-month total PCS: r = −.206, p = .007; 1-week Visual Memory composite with 3-month total PCS: r = −.129, p = .097). Therefore, giving consideration to the potential for multicollinearity and the limitations on the number of variables that could be included in the regression analyses, these were the two cognitive measures from ImPACT selected for use in the regressions.

Examination of the intercorrelations of predictor variables revealed that initial GCS was significantly associated with PTA duration (r = .572, p < .001). To avoid multicollinearity, we did not include GCS in the analyses, because PTA showed a stronger association with PCS. The preinjury SF-36 Mental Component score was significantly correlated with the SF-36 Physical Component score (−.328, p < .001) and with preinjury MINI neuro-psychiatric status (−.377, p < .001). Because the latter showed a stronger correlation with PCS, the SF-36 Mental Component score was excluded from the regressions. Additionally, there were significant correlations between the HADS anxiety and depression scores (r = .670, p < .001). Because HADS anxiety was more strongly associated with PCS, to avoid multicollinearity, we included only the HADS anxiety score as a predictor.

**Prediction of 1-Week PCS From Preinjury and Acute Injury Predictors**

For Model 1a (ED/acute predictors), the significant predictors of a higher PCS score at 1-week postinjury were having had a mTBI, gender and preinjury psychiatric history, with participants with mTBI (odds ratio [OR] = 3.25, p = .001), women (OR = 2.56, p = .004), and those with psychiatric history (OR = 3.7, p < .001) at a higher risk of PCS at 1 week. Other variables used in the model that were not significantly predictive were acute cognitive memory measures (ImPACT Verbal Memory score, acute ImPACT Visual Memory score), as well as PTA duration, age, and preinjury SF-36 Physical Health.

**Prediction of 3-Month PCS From Preinjury and Acute Injury Predictors**

For Model 1b (ED/acute predictors), the significant predictors of higher PCS score at 3 months postinjury were presence of preinjury psychiatric history (OR = 2.56, p = .006) and lower preinjury Physical Health on the SF-36 (OR = 1.09, p = .004), with mTBI no longer a significant predictor. Again, acute cognitive measures of memory as well as Group (mTBI vs. TC), gender, age, and PTA duration were not associated with PCS at 3 months.

**Prediction of PCS at 1 Week From Injury-Related and Concurrent Measures at 1 Week**

For Model 2a (1-week variables), the significant predictor of a higher PCS score at 1 week were having had a mTBI (OR = 3.30, p < .001), more anxiety symptoms on the HADS (OR = 1.32, p < .001), and greater pain severity on the VAS (OR = 1.03, p < .001). Again, 1-week ImPACT Verbal Memory and Visual Memory scores—as well as gender, age, preinjury SF-36 Physical Health, PTA duration, and 1-week narcotic analgesia—were not significantly predictive.

**Prediction of PCS at 3 Months From Injury-Related and 1-Week Variables**

For Model 2b (1-week variables predicting outcome at 3 months), having a mTBI was no longer a significant predictor of higher PCS score at 3 months postinjury. However, presence of more anxiety symptoms on the HADS at 1 week remained a highly significant predictor of 3-month PCS (OR = 1.18, p < .001). One-week assessments on ImPACT Verbal and Visual Memory measures as well as gender, age, preinjury SF-36 Physical Health, PTA duration, and VAS pain at 1 week were not significant predictors of 3-month PCS.

**Prediction of PCS at 3 Months From Injury-Related and Concurrent 3-Month Variables**

For Model 3 (3-month variables), again having a mTBI was no longer a significant predictor of 3-month PCS, nor were 3-month ImPACT Verbal and Visual Memory scores, gender, age, preinjury SF36 Physical Health, or PTA duration. The significant concurrent predictors or indicators were a higher anxiety symptom score on the HADS (OR = 1.31, p = .002), greater VAS pain severity (OR = 1.04, p = .04), presence of more PTSD symptoms on the PCLS (OR = 1.09, p = .03), and other stressful life events on the RSRRS (OR = 1.001, p = .02).

**Prediction of PCS at 3 Months for mTBI and Trauma Control Groups Separately**

The final models examined predictors of PCS at 3 months postinjury for each group separately. In the model including only mTBI participants, the significant predictors were HADS anxiety symptoms (OR = 1.42, p = .01) and higher age (OR = 1.07, p = .04). In the model including only TC participants, the significant predictors were presence of PTSD symptoms on PCLS (OR = 1.23, p = .04) and other life stressors on the RSRRS (OR = 1.001, p = .02). Three-month ImPACT Verbal and Visual Memory scores, along with gender, preinjury SF-36 Physical health, PTA duration, and 3-month VAS pain, were not significant predictors of 3-month PCS in either group.
An analysis of the bivariate relationship between the presence of preinjury psychiatric disorders and HADS scores 1 week and 3 months postinjury revealed that HADS anxiety scores at 1 week were associated with greater likelihood of a preinjury psychiatric disorder, \( t(1, 75) = -2.500, p = .013 \), whereas HADS Depression scores did not show such an association. HADS anxiety and depression scores at 3 months postinjury were not significantly associated with preinjury psychiatric disturbances.

**Discussion**

This study of predictors of outcome in individuals with uncomplicated mTBI and general trauma not requiring surgery found that mTBI predicted PCS during the acute phase after injury, but not at 3 months postinjury. It also found that premorbid psychiatric factors and postinjury anxiety were the strongest predictors of persistent symptoms at 3 months postinjury.

Three factors contributed uniquely to reporting of PCS at 1 week after injury—namely, having experienced a mTBI, presence of a preinjury psychiatric disorder, and being female. The finding is in some respects consistent with the findings of Meares and colleagues (2008) in identifying the association between preinjury psychiatric disturbance, female gender, and reported PCS soon after injury. However, the present study, by focusing on trauma groups who were well-matched but had less-complex injuries and had had no surgery since injury, has identified that the experience of a mTBI also renders the person more than three times as likely to experience PCS in the first week postinjury than a general trauma patient without mTBI. Therefore it would seem erroneous to conclude that mTBI does not cause PCS in the early days after injury. As has been found in some previous studies, one of the traditional markers of injury severity, namely, duration of PTA, was not associated with reported PCS either at 1 week or 3 months after injury. Moreover, performance on the ImPACT cognitive concussion battery, specifically the Verbal and Visual memory modules, also failed to predict PCS both at 1 week and 3 months postinjury (Carroll et al., 2004; Meares et al., 2006, 2008; Ponsford et al., 2000; Stulemeijer, van der Werf, Borm, & Vos, 2008), despite the fact that mTBI participants did perform more poorly on the ImPACT Visual Memory index at both of these time points. Some previous studies have found other neuropsychological tests to be sensitive to effects of mTBI in the early stages after injury, including tests of visual RT, Digit Symbol Coding, the Speed of Comprehension Task, and Paced Auditory Serial Addition Task when administered in the early days after injury, with some studies also showing impairment on tests of visual or verbal memory (Carroll et al., 2004; Kwok, Lee, Leung, & Poon, 2008; Malojicic, Mubrin, Coric, Susnic & Spilich, 2008; Peterson et al., 2009; Ponsford et al., 2000; Vanderploeg, Curtiss, & Belanger, 2005). However, there is limited evidence that administration of these tests is predictive of PCS in either the short or the long term. The administration of computerized neuropsychological tests in the acute setting does not appear to be helpful in the management of patients with uncomplicated mTBI.

Neither education nor history of previous head injury was associated with PCS at 1 week or 3 months postinjury. Older age emerged as a predictor in the mTBI group only at 3 months postinjury. It was also clear that litigation was not a factor that contributed to reporting of PCS. This possibly reflects the low proportion of participants engaged in litigation. The influence of litigation may only appear when recruitment occurs in that context, as was the case in the study by Mooney and colleagues (2005).

PCS reporting was more strongly associated with the injured person’s anxiety levels at 1 week postinjury, which was in turn associated with preinjury psychiatric history. It is possible that the experience of PCS resulted in heightened anxiety in individuals with a psychiatric history, who may have greater anxiety sensitivity and less adaptive coping mechanisms or stress tolerance. The symptoms experienced then caused anxiety, which might have further exacerbated symptoms. In support of this contention is the finding that reporting more anxiety symptoms on the HADS at 1 week postinjury was associated with greater likelihood of persisting PCS 3 months postinjury.

This finding supports that of previous studies by Dischinger et al. (2009) in which early symptoms of anxiety, noise sensitivity, and trouble thinking predicted long-term PCS 3 months postinjury, with women who reported anxiety early after injury being most likely to develop ongoing PCS. Stulemeijer and colleagues (2008) also found that emotional distress was significantly associated with continuing cognitive complaints 6 months postinjury, along with lower education, personality, and poor physical functioning, especially fatigue. This suggests that individuals showing high levels of anxiety symptoms early after injury may be targeted for preventative intervention. As suggested by Mittenberg, Tremont, Zielinski, Fichera, and Rayles (1996), the injured person’s appraisal or attribution of symptoms may play a role in perpetuating them. Mittenberg and colleagues (1996) and Cicerone (2002) have advocated for the use of cognitive behavior therapy (CBT) to encourage patients to change their inner dialogue to develop a sense of mastery over symptoms and take control of their lifestyle, by using thought stopping, replacing negatively biased thoughts, and encouraging return to rewarding activities. Hodgson and colleagues (Hodgson, McDonald, Tate, & Gertler, 2005) showed that CBT may reduce social anxiety following mTBI. While Ghaffar, McCullagh, Ouchterlony, and Feinstein (2006) found no significant overall advantage in the provision of routine multidisciplinary treatment and follow-up to all individuals with mTBI, individuals with preexisting psychiatric problems did benefit from the intervention. We would therefore propose that individuals with a history of psychiatric disorder and those showing high levels of anxiety at 1 week after mTBI may be targeted for cognitive-behavioral interventions. There is a need for further evaluation of such intervention models, however.

By 3 months postinjury the experience of a mTBI did not contribute uniquely to reported PCS, which was most strongly associated with the experience of PTSD symptoms and other stressors, anxiety, and pain. However, it should be noted that the frequency of a score indicative of a formal diagnosis of PTSD was not high in either group \((n = 7 \text{ in mTBI and } 3 \text{ in TC group})\). Moreover, the fact that the predictors of PCS differed between the mTBI and TC groups at 3 months postinjury suggests that there may have been differing sources of anxiety, with PTSD symptoms and other life stressors most significant for the TCs, but older age and the presence of anxiety on the HADS showing a stronger association for mTBI participants. The higher HADS anxiety scores may have been a response to the experience of injury-related symptoms. This is also supported by the finding of greater self-reported concentration and memory difficulties affecting daily activities in the mTBI group in relation to TCs, as
reported by Ponsford and colleagues (2011). However, one cannot be sure of the direction of this association, and further investigation of this is warranted.

This study focused on individuals with mTBI with no focal neurological signs, nor evidence of injury on CT scan and who were not under the influence of illicit substances or requiring general anesthesia. We did this to exclude extraneous causes of cognitive impairment. This sample represents the very mildest end of the mTBI spectrum and cannot be said to represent individuals with complicated mTBI for whom predictors of outcome may differ. The sample who participated was also slightly older than the group that did not agree to participate, and one cannot rule out the possibility that this in some way influenced the findings, given that age proved to be a significant predictor in the model predicting 3-month outcome in the TBI group. Moreover, given the number of statistical comparisons, we cannot rule out the possibility of Type I error.

Taking into account these factors, we believe that this study has demonstrated that the presence of a mTBI does contribute significantly to PCS within the acute stages after injury in patients with uncomplicated trauma, but not to longer-term PCS, which were more strongly predicted by premorbid psychiatric factors and postinjury anxiety. Individuals with a preinjury psychiatric history appear to respond to the experience of mTBI and PCS with greater anxiety, which may, in turn, exacerbate their PCS. The effects of mTBI are thus complex and multifactorial. If we are to improve management of this condition, we need to acknowledge this complexity, and equip individuals with information and coping strategies to minimize the development of anxiety.

References


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