

# Characterizing Self-Reported Sleep Disturbance after Mild Traumatic Brain Injury

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## Abstract

Sleep disturbance after mild traumatic brain injury (mTBI) is commonly reported as debilitating and persistent. However, the nature of this disturbance is poorly understood. This study sought to characterize sleep after mTBI compared with a control group. A cross-sectional matched case control design was used. Thirty-three persons with recent mTBI (1–6 months ago) and 33 age, sex, and ethnicity matched controls completed established questionnaires of sleep quality, quantity, timing, and sleep-related daytime impairment. The mTBI participants were compared with an independent sample of close-matched controls (CMCs;  $n=33$ ) to allow partial internal replication. Compared with controls, persons with mTBI reported significantly greater sleep disturbance, more severe insomnia symptoms, a longer duration of wake after sleep onset, and greater sleep-related impairment (all medium to large effects, Cohen's  $d>0.5$ ). No differences were found in sleep quantity, timing, sleep onset latency, sleep efficiency, or daytime sleepiness. All findings except a measure of sleep timing (i.e., sleep midpoint) were replicated for CMCs. These results indicate a difference in the magnitude and nature of perceived sleep disturbance after mTBI compared with controls, where persons with mTBI report poorer sleep quality and greater sleep-related impairment. Sleep quantity and timing did not differ between the groups. These preliminary findings should guide the provision of clearer advice to patients about the aspects of their sleep that may change after mTBI and could inform treatment selection.

**Key words:** concussion; excessive daytime sleepiness; insomnia; post-concussion syndrome

## Introduction

SLEEP DISTURBANCE is a common complaint in mild, moderate, and severe traumatic brain injury (TBI).<sup>1,2</sup> A recent meta-analysis of 21 studies examining the prevalence of sleep disturbance after TBI found that an average of 50% of persons post-TBI experienced some type of sleep disturbance.<sup>1</sup> Sleep complaints are particularly prominent after mild TBI (mTBI), and are described by patients as one of the most debilitating post-injury symptoms.<sup>3</sup>

The significance of sleep complaints after mTBI is not well understood. Although the base rate of such complaints is high in the general population,<sup>4</sup> it is possible that when they occur after mTBI, they indicate sleep disturbance sufficient to worsen physical and mental recovery.<sup>5–8</sup> For example, sleep disturbance could: contribute to or exacerbate comorbid conditions such as depression, fatigue and pain<sup>1,9</sup>; worsen recovery because the normal restorative and recuperative functions of sleep are disrupted<sup>3</sup>; interfere directly with rehabilitation<sup>5</sup>; or signal ongoing disruption of neurophysiological processes.<sup>6,10,11</sup> It is possible that sleep disturbance before the TBI is also a contributor to poor outcome by increasing vulnerability or reducing recovery capacity.

It has been acknowledged that the term “sleep disturbance” is poorly defined in the TBI literature.<sup>1</sup> Some studies use the term sleep disturbance to indicate disruption to any one aspect of sleep, such as sleep duration,<sup>8</sup> while others use it to indicate the presence of clinical sleep disorders.<sup>12</sup> Although it is possible to identify specific types of sleep disturbance and to determine whether disorder thresholds are breached, many mTBI studies do not report these details, and there is significant variation in the reporting of sleep characteristics.<sup>1</sup> As such, drawing conclusions from the existing published studies of sleep disturbance and mTBI is difficult and must be done cautiously.

Many of the previous sleep and TBI studies have important limitations.<sup>1</sup> These limitations include: failing to include a control group when one is required; using a mixed severity TBI sample or failing to identify/explain/use standard diagnostic criteria; recruiting patients with TBI from sleep disorder treatment settings, which may introduce a selection bias; or, failing to control or restrict the time since injury meaning that acute and chronic presentations are confounded. Further, there is significant variation in the use of outcome measures, making comparisons across studies difficult, and although most studies have used subjective sleep measures

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(questionnaires), in some cases, this has been suboptimal (e.g., the use of a single, potentially confounded questionnaire item, such as “difficulty falling or staying asleep”).<sup>13</sup> A summary of the past literature in this area is shown in Table 1. Table 1 illustrates the findings from these previous studies and highlights methodological variations.

Very few past TBI studies have examined more than two facets of sleep. As Table 1 shows, sleep quality is the most commonly investigated facet of subjective sleep after mTBI, and most studies suggest that this worsens after the injury. There are several facets of sleep that can be differentiated to allow for better characterization of the patient experience. This characterization is important to assist with the identification of etiology and to guide treatment to improve sleep. Sleep disturbance can affect sleep quality, quantity, or the timing of sleep, and it can also be inferred from the presence of daytime impairment (e.g., excessive daytime sleepiness).

The purpose of this study was to characterize four facets of sleep (sleep quality, quantity, timing, and daytime impairment) in a sample with mTBI and matched controls. A better understanding of sleep disturbance after mTBI may help determine which, if any, interventions are indicated in this population. Sleep disturbance is often treatable, despite its initial cause,<sup>14</sup> and treating sleep complaints may help improve outcomes such as neuropsychological functioning in persons with mTBI.<sup>7</sup> Based on previous research, it was predicted that persons who had sustained an mTBI would report (1) poorer subjective sleep quality; (2) longer sleep onset latency (SOL); (3) increased wake after sleep onset (WASO), (4) poorer sleep efficiency, and (5) would experience more severe insomnia symptoms than would controls. It was also expected that habitual sleep duration would be reduced after mTBI compared with controls. No differences in sleep timing (i.e., habitual bedtime and waketime and bedtime and waketime stability) and no differences in daytime impairment (sleep-related impairment or daytime sleepiness) were expected, as neither circadian rhythm disorders nor increased subjective report of sleepiness after mTBI have been consistently demonstrated.

## Methods

### Participants

**Recruitment and screening.** Undergraduate students from Queensland University of Technology and members of the general community were recruited via snowball sampling (e-mail and flyer advertisements that encouraged participants to forward the study information to others). People aged 17 years and older were invited to participate if they had: experienced an mTBI between 1 and 6 months ago or had no history of mTBI. A total of 41 people who had recently sustained an mTBI and 223 people with no history of mTBI had valid data ( $N=264$ ).

Twenty-six participants were removed because they failed the exclusion criteria ( $n=8/41$  mTBI,  $n=18/223$  controls). These criteria excluded participants who (a) had sought treatment in the last 12 months for a mental/intellectual impairment (e.g., severe brain injury, seizures, or other neurological problems) or a psychological/psychiatric disorder (e.g., depression:  $n=12$ ; three persons with mTBI); (b) had a current self-reported sleep disorder (i.e., narcolepsy, sleep apnea, or “other”:  $n=10$ ; three persons with mTBI); or (c) failed two or more instructional manipulation checks for indiscriminate responding ( $n=1$  control). An additional three participants were excluded on multiple criteria: one control participant was excluded based on criteria 2 and 3, and two participants with mTBI were excluded for failing criteria 1 and 2, or all three criteria, respectively.

**mTBI sample.** After screening, the mTBI sample consisted of 33 participants (19 female), aged 17–41 years (Mean [M]=22.25,

standard deviation [SD]=5.72). The primary cause of the mTBI was sport-related ( $n=22$ ), followed by: a fall ( $n=8$ ), a motor vehicle accident ( $n=1$ ), an assault ( $n=1$ ) or “other” (not specified;  $n=1$ ). Although 22 persons sustained a sport-related mTBI and the majority of the sample were students, this study did not specifically recruit “college athletes.” Fourteen participants reported experiencing a previous “concussion” (number of concussions range = 2–5,  $M=3.3$ ,  $SD=1.16$ ,  $n=10$ ; missing  $n=4$ ). Eight persons had current pain from the injury, where the average severity of pain was 2.85 on a 1–10 scale (range = 1–8;  $M=3.92$ ;  $SD=2.23$ ;  $n=12$ ).

Participants self-reported experiencing an mTBI based on the following statement adapted from the World Health Organization’s operational definition of mTBI<sup>15</sup>:

These statements will ask you about any concussion you may have had. By ‘concussion’ we mean an acute brain injury resulting from mechanical energy to the head from external physical forces. Concussion can result from things like playing sports, motor vehicle accidents, assaults and falls. Symptoms include at least one of the following: Confusion or disorientation (e.g., not knowing where you are or what day it is); Loss of consciousness for 30 min or less; Being unable to remember events that occurred after the blow to the head for less than 24 h. Please indicate if and when you have experienced a concussion according to the above definition (we are interested in your most recent concussion).

**Matched controls.** Thirty-three participants were selected from the pool of 205 respondents with no history of mTBI. Case-control studies and individual matching are a means of decreasing bias from known confounds,<sup>16–18</sup> and this method has been used previously in TBI research on sleep.<sup>19,20</sup> Control participants were selected using the MatchIt optimal matching package from the statistical software program, R (Version 2.15.2).<sup>21</sup> This process finds the best possible fit of controls to cases by minimizing an overall distance measure, based on the chosen covariates. Three covariates were used: sex, age (within 5 years), and ethnicity (Caucasian, non-Caucasian). This process resulted in the identification of one control for each case that was matched on age (except one case with missing age), sex, and ethnicity.

**Close-matched controls (CMCs).** Using the same optimal matching process, a second independent sample ( $n=33$ ) was drawn from the remaining pool of 172 respondents with a negative history of mTBI. This pool was less optimally matched to mTBI cases than the control sample. The CMC group was drawn to allow a further test of the hypotheses via partial internal replication. This approach has been used previously,<sup>22</sup> and it is consistent with recent recommendations that strongly encourage the use of replication.<sup>23,24</sup> Where possible, CMCs were matched within 5 years of age. Six participants had a greater than 5-year age difference between case and controls. Of these six participants, three were not a match on ethnicity, and one was not a match on sex. One case with missing age was matched only on sex and ethnicity.

The demographic characteristics of all three groups are shown in Table 2. Between-groups comparisons (mTBI vs. controls, mTBI vs. CMCs) generally revealed no significant differences on key background variables, including self-reported stimulant/sedative use and feelings of depression or anxiety. The one exception was a group difference on the number of nights of sleep disturbed by pain (mTBI > controls; mTBI > CMCs).

### Measures

#### Sleep quality

*Patient-Reported Outcomes Information System (PROMIS) Sleep Disturbance-Short Form 8b, Version 1.0 (PROMIS8b)*<sup>25</sup>. The PROMIS8b sleep scale is part of a relatively new

TABLE 1. SUMMARY OF RESEARCH OF SLEEP DISTURBANCE IN TRAUMATIC BRAIN INJURY IN ADULTS IN CHRONOLOGICAL ORDER

Ref. no.	Study	Sample	Injury severity for TBI severity	Sleep treatment seeking sample?	Time since injury	Sleep aspect	Methodology	Key findings
8	Mahmood et al., 2004	87 TBI patients. No control group	Mild-severe	No. Recruited outpatients at neuro rehabilitation unit. Exclusion criteria: sleep medication use.	<1 year	Quality	Self-report; PSQI	Self-report: 37% reported sleep disturbance; mild TBI reported more sleep disturbance than moderate-severe TBI (not because of having more pain, litigation, depression, or time since injury). mTBI reported significantly worse subjective sleep quality; shorter quantity and more specific sleep disturbances than severe TBI.
51	Steele et al., 2005	10 TBI patients + 10 matched controls	Mild-severe	No. Recruited at routine review appointment in rehabilitation unit. Exclusion criteria: symptoms of pre-injury sleep disorders, unhealthy BMI, travel >1 time zone in last 3 months, shift work, sedative use, insufficient English, previous head injury or psychiatric condition.	74-1194 days	Timing	Self-report: MEQ. sleep diary Objective: Salivary melatonin	Self-report: 7 TBI patients reported change to bedtime (earlier/later) from pre- to post-injury compared with 1 control (3 months prior). No differences in bed/wake times between groups (sleep diary), or circadian type on MEQ. Objective: No significant difference in circadian timing between TBI and controls.
63	Parcell et al., 2006	63 TBI patients + 63 matched controls	Mild-severe	No. Recruited 2 weeks after hospital discharge. Exclusion criteria: sleep medication use, insufficient English, travel >1 time zone in last 3 months, shift work last 12 months, pre-injury sleep disorder, sedative use, previous head injury or psychiatric disorder.	20-1194 days (M = 230)	Quality Timing	Self-report: Sleep-wake diary, ESS, General Sleep Questionnaire	Self-report: TBI group reported significantly more change to their sleep quality (increased WASO & SOL) and timing from pre to postinjury, compared with controls (3 mths prior). No significant difference between groups in daytime sleepiness. TBI group reported poorer SE, later waking and longer naps during weekdays than controls.

(continued)

TABLE 1. (CONTINUED)

Ref. no.	Study	Sample	Injury severity for TBI severity	Sleep treatment seeking sample?	Time since injury	Sleep aspect	Methodology	Key findings
2	Ouellet et al., 2006	452 TBI patients. No control group	Mild-severe	No. Broad recruitment.	M = 7.85 years	Quality	<i>Self-report:</i> ISI, MFI, Sleep and Fatigue questionnaires, partner questionnaire <i>Self-report:</i> MEQ <i>Objective:</i> Actigraphy, PSG, melatonin measured, temperature rhythm	<i>Self-report:</i> 50% reported insomnia symptoms; 29% met diagnostic criteria – slightly higher in mild TBI (38%) than moderate (35%) and severe (24%). <i>Self-report:</i> Confirmation of circadian type in majority participants. <i>Objective:</i> 36% of participants presenting with insomnia diagnosed with CRSD – PSG ruled out other sleep disorders. Eight persons had DSPS and seven ISWP. Overall, 76% of TBI patients had some sleep-wake disturbance –EDS, fatigue and hypersomnia were common. <i>Self-report:</i> 28% reported excessive daytime sleepiness on ESS <i>Objective:</i> 25% had objective findings of excessive daytime sleepiness (MSLT).
52	Ayalon et al., 2007	42 mTBI patients. No control group	Mild	Yes. Complaints of insomnia and daytime fatigue	Not described	Timing		
64	Baumann et al., 2007	65 TBI patients. No control group	Mild-severe	No. Exclusion criteria: pre-injury sleep-wake disorder or psychiatric condition.	6 months	Sleepiness Quantity	<i>Self-report:</i> Interview, re sleep disturbances and sleepiness, ESS, SA-SDQ, Ullanlinna Narcolepsy scale, Swiss Narcolepsy Scale <i>Objective:</i> PSG, MSLT	
65	Castriotta et al., 2007	87 TBI patients. No control group	Mild-severe	No. Recruitment from rehabilitation unit. Exclusion criteria: CRSD sedative use, inability to provide informed consent.	55 people: 3–36 mths, 32 people: more than 36 months	Sleepiness	<i>Self-report:</i> ESS <i>Objective:</i> PSG, MSLT	<i>Self-report:</i> High prevalence of sleepiness (25%) and sleep disorders (46%) in persons with TBI. <i>Objective:</i> High prevalence of sleepiness measured by MSLT score <10 (26%). No difference depending on injury-severity.
66	Chandra et al., 2007	10 TBI patients + 10 matched controls	Not described	No. Outpatient review appointment in rehabilitation unit and general population. Exclusion criteria: not described.	“sub-acute”	Timing	<i>Self-report:</i> MEQ, sleep diary	<i>Self-report:</i> TBI and controls reported similar average sleep times. Change in sleep timing reported by TBI participants comparing post- to pre-injury retrospectively.

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TABLE 1. (CONTINUED)

Ref. no.	Study	Sample	Injury severity for TBI severity	Sleep treatment seeking sample?	Time since injury	Sleep aspect	Methodology	Key findings
47	Schreiber et al., 2008	26 mTBI patients + 26 matched controls	Mild	Yes. TBI referred to sleep lab for complaints of poor sleep. Exclusion criteria: past CNS impairment, psychiatric disorder, sleep apnea or RLS. Yes. mTBI included if they had sleep disturbances within a month post-injury and SOL > 30 mins for 4 days/week.	1–21 yrs	Quality Sleepiness	Objective: PSG, MSLT	Objective: Shorter sleep duration (TST). More stage 2 and less REM in mTBI, as well as increased sleepiness on MSLT compared with controls.
45	Williams et al., 2008	9 mTBI patients + 9 controls	Mild	Yes. mTBI included if they had sleep disturbances within a month post-injury and SOL > 30 mins for 4 days/week.	M = 27.8 months	Quality	Self-report: PSQI, SDQ, BSIQ, Sleep Diary Objective: PSG	Self-report: Poorer sleep quality, increased SOL and disturbances in mTBI patients postinjury and compared to controls. Participants reported a decrease in sleep duration compared to preinjury. No differences in duration or daytime sleepiness compared to controls. Objective: mTBI patients had longer SOL, more than twice as long as controls.
9	Chaput et al., 2009	443 mTBI patients. No control group.	Mild	No. Any patient (> 16 years old) seen in hospital > 1 day duration, symptoms not from intoxication or other injuries. Exclusion criteria: intellectual disability, dementia, learning impairment, or psychiatric disorder.	Not described	Quality	Self-report: Symptom complaints reported and classified as: pain related, WASO, increased sleep, difficulty falling asleep, nightmares, headache	Self-report: At 6 weeks fatigue (34.6%) and sleep complaints (33.5%) second and third most common complaints after headaches. Patients with sleep complaints more likely to have headaches, depressive symptoms, and irritability.
19	Gosselin et al., 2009	10 mTBI patients + 11 matched controls	Mild	No. No history or laboratory studies indicating sleep disturbances. Exclusion criteria: neurological/psychiatric disorder, extremely early or late bedtimes, medication use affecting sleep/wake, shift work or travel across time zones in past 2 months.	< 1 year	Quality Timing	Self-report: PSQI, ESS Objective: PSG	Self-report: Worse sleep quality on PSQI: sleep quality, disturbance, and daytime dysfunction subscales significant. Longer SOL reported by mTBI, but no difference in bedtime, duration, or daytime sleepiness. Significantly higher depression in mTBI Objective: No significant difference on any measures (e.g. SOL, WASO, or sleep duration).

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TABLE 1. (CONTINUED)

Ref. no.	Study	Sample	Injury severity for TBI severity	Sleep treatment seeking sample?	Time since injury	Sleep aspect	Methodology	Key findings
67	Kempf et al., 2010	51 TBI patients. No control group	Mild-severe	No. Exclusion criteria: pre-injury neurological/psychiatric disorder, sleep-wake disorder, or previous head injury.	3 years	Quality Sleepiness	Self-report: Phone interview, ESS, SA-SDQ, the Ullanlinna narcolepsy scale, the Swiss Narcolepsy Scale, the Fatigue Severity Scale	Self-report: 67% had posttraumatic SWD 3yrs postinjury, 63% fatigue, sleepiness, hypersomnia and 10% insomnia. In 45% could not find other cause of SWD than the injury
11	Rao et al., 2011	7 mTBI patients + 7 matched controls	Mild	No. General population approached. Exclusion criteria: pre-injury neurological or sleep disorder, intellectual disability, open head injury, psychotropic drug use in last month, history of alcohol abuse, prisoner, or poor physical health.	<1 week	Quality Quantity	Objective: PSG, PSA of EEG	Objective: No significant differences (N=14), trend toward delayed SOL, longer WASO, shorter Stage 2 and less TST.
68	Scheckleton et al., 2010	23 TBI patients + 23 matched controls	Mild-severe	No. Recruited from rehabilitation unit. Exclusion criteria: pre-injury sleep disorder, neurological/psychiatric disorder, insufficient English, sleep medication use, shift work in last 3 years, travel across time zones in the last 3 months.	6 months	Quality Sleepiness	Self-report: PSQI, ESS, MEQ Objective: PSG, salivary dim light melatonin onset time	Self-report: TBI reported poorer sleep on the PSQI, after controlling for anxiety and depression. Objective: TBI patients reported more WASO and poorer SE than controls after controlling for anxiety, weakened after controlling for depression. TBI patients had lower levels of evening melatonin production.
20	Beaulieu-Bonneau & Morin, 2012	22 TBI patients + 22 matched controls	Moderate-severe	No. Recruited from rehabilitation centers with past or current driver's license. Exclusion criteria: medical condition causing sleepiness/cognitive impairment, sensory or motor impairment, bipolar or psychotic or depressive disorder, sleep apnea, use of hypnotic medication, shift work in the last year, unusual bed- and/or wake times.	1-11 years (M=4.42 years)	Sleepiness	Self-report: ESS, FOSQ, MFI, VAS-S, VAS-F, Sleep Diary, ISI Objective: PSG, MWT	Self-report: No differences in sleepiness between the groups on ESS but reported poorer consequences of sleepiness on FOSQ, spent more time in bed at night, and took more naps during the day. Objective: No difference on sleepiness measured by MWT, no difference on PSG measure or sleep diary.

(continued)

TABLE 1. (CONTINUED)

Ref. no.	Study	Sample	Injury severity for TBI severity	Sleep treatment seeking sample?	Time since injury	Sleep aspect	Methodology	Key findings
46	Khoury et al., 2012	24 mTBI patients + 18 controls	Mild	No. Exclusion criteria: severe cognitive or speech impairment, psychotropic medication use, neurological/psychiatric conditions, alcohol abuse, pre-injury chronic pain or sleep disorders.	<6 wks	Quality Quantity	Self-report: PSQI, VAS Objective: PSG, PSA EEG	Self-report: mTBI patients reported three times poorer scores on PSQI than controls. Objective: Sleep architecture differences between groups, but within normal range. EEG revealed some differences between groups. Pain associated with poorer sleep quality. Self-report: Significantly poorer sleep in TBI group, greater daytime sleepiness.
69	Ponsford et al., 2012	140 TBI patients + 140 controls	Mild-severe	No. (not described)	3 weeks – 3 years (M=9.71 months)	Quality Sleepiness	Self-report: PSQI, FSS, ESS	Self-report: 38% reported general sleep disturbance after TBI; 29% insomnia and 9% hypersomnia. Insomnia most common in moderate TBI and hypersomnia in severe TBI. Self-report: Insomnia symptoms were improved after individualized intervention (e.g. sleep hygiene, medication, sleep apnea treatment)
70	Hou et al., 2013	98 TBI patients. No control group	Mild-severe	No. Recruited through hospital Exclusion criteria: sedative use, shift work, preinjury sleep and/or psychiatric disorders.	M=33 months (SD=11)	Quality Sleepiness	Self-report: PSQI, ESS, (HADS), and symptom questions)	Self-report: 38% reported general sleep disturbance after TBI; 29% insomnia and 9% hypersomnia. Insomnia most common in moderate TBI and hypersomnia in severe TBI.
7	Wiseman-Hakes et al., 2013	10 TBI patients No control group	Mild-severe	Yes. Participants (18–60 years old) included if reporting sleep and/or wake disturbance, ISI score > 15 (clinical insomnia), communication impairments, sufficient functioning to understand the study, sufficient English, and being able to supply consent.	1–22 yrs	Quality Quantity	Self-report: ISI, DCCASP, ESS Objective: PSG, MWT	Self-report: Insomnia symptoms were improved after individualized intervention (e.g. sleep hygiene, medication, sleep apnea treatment)

mTBI, mild traumatic brain injury; GCS, Glasgow Coma Scale; LOC, loss of consciousness; PSQI, Pittsburgh Sleep Quality Index; PTA, post-traumatic amnesia; CT, computed tomography; BMI, body mass index; MEQ, Morningness-Eveningness Questionnaire; ESS, Epworth Sleepiness Scale; MRI, magnetic resonance imaging; ISI, Insomnia Severity Index; MFI, Multidimensional Fatigue Inventory; PSG, polysomnography; CRSD, Circadian Rhythm Sleep Disorders; PSG, polysomnography; DSPPS, Delayed Sleep Phase Syndrome; ISWP, irregular sleep-wake pattern; GOS, Glasgow Outcome Scale; SA-SDQ, Sleep Apnea Scale of the Sleep Disorders questionnaire; EDS, excessive daytime sleepiness; MSLT, Multiple Sleep Onset Latency Test; EEG, electroencephalography; CNS, central nervous system; RLS, restless legs syndrome; TST, total sleep time; REM, rapid eye movement; SDQ, sleep disorders questionnaire; BSIQ, Brock Sleep and Insomnia Questionnaire; SOL, Sleep Onset Latency; WHO, World Health Organization; WASO, wake after sleep onset; ACRM, American Congress of Rehabilitation Medicine; PSA of EEG, Power Spectral Analysis of EEG; SE, sleep efficiency; FOSQ, Functional Outcomes of Sleep Questionnaire; VAS-S, Visual Analogue Scale for Sleepiness; VAS-F, Visual Analogue Scale for Fatigue; ISI, Insomnia Severity Index; MWT, Maintenance of Wakefulness Test; FSS, Fatigue Severity Test; SD, standard deviation; HADS, Hospital Anxiety and Depression Scale; DCCASP, Daily Cognitive-Communication and Sleep Profile.

TABLE 2. DESCRIPTIVE STATISTICS FOR PARTICIPANT CHARACTERISTICS AND BETWEEN-GROUP COMPARISONS

	1. mTBI (n=33)	2. Control (n=33)	3. CMC (n=33)	1 vs 2 p (2-tailed)	1 vs 3 p (2-tailed)
Age: M (SD)	22.25 (5.72)	21.81 (5.36)	23.27 (9.76)	0.748	0.881
Male (n)	14	14	15		
Female (n)	19	19	18	1.00	1.00
Caucasian (n)	29	29	26	1.00	0.325
Dominant language: (n)					
English	30	28	31	0.708	1.00
Years of education: M (SD)	14.03 (2.36)	13.76 (2.15)	14.58 (2.67)	0.390	0.331
Currently enrolled in tertiary education: (n)	29	32	31	0.355	0.672
Caffeine consumption: M (SD)					
Drinks/morning:	0.79 (0.65)	0.75 (0.87)	1.58 (0.66)	0.580	0.187
Drinks/afternoon:	1.48 (0.63)	1.57 (0.92)	1.72 (0.66)	0.978	0.298
Drinks/evening:	1.34 (0.67)	1.50 (0.92)	1.39 (0.50)	0.630	0.511
Frequency that sleep is disturbed by pain/discomfort: M (SD)	2.88 (1.02)	2.30 (1.02)	2.40 (1.10)	0.015	0.026
Sleep medication use (n)	3	0	1	0.238	0.613
Stimulant use (n)	2	1	0	1.00	0.492
Sedative use (n)	0	2	0	0.492	0.492
Depressed or sad: M (SD) <sup>b</sup>	1.28 (1.08)	1.09 (1.06)	1.27 (1.11)	0.430	0.903
Anxious or tense: M (SD) <sup>b</sup>	1.16 (1.19)	0.88 (1.01)	0.87 (0.97)	0.361	0.386

N=99. mTBI, mild traumatic brain injury; CMC, close-matched controls; SD, standard deviation.

Between-group comparisons were performed using Mann-Whitney *U* tests for continuous variables and chi-square tests for categorical tests (with a Fischer exact correction applied for analyses with violated assumptions).

<sup>a</sup>Frequency that sleep is disturbed by pain or discomfort was measured on a 5-point scale (1=Never, 2=Rarely, 3=A few nights a month, 4=A few nights a week, 5=Every night or Almost every night).

<sup>b</sup>Items taken from the Neurobehavioral Symptom Inventory, which are measured on a 5-point scale (0=not at all, 4=very severe).

group of physical and mental health measures drawn from the United States of America National Institutes of Health's framework to address limitations of existing patient report measures.<sup>25,26</sup> Commentaries about these measures have been published recently,<sup>27</sup> and their potential as a common outcome measure in TBI research has been suggested.<sup>28</sup>

The PROMIS8b is a reliable measure of general subjective sleep disturbance that asks participants to rate their general sleep over the past 7 days. A 5-point rating scale appropriate to the item is used; for example, "my sleep was restless" (not at all - very much), "I had trouble staying asleep" (never - always), and "my sleep quality was" (very poor - very good). Items 2, 3, 7, and 8 are reversed and all items summed for a total score ranging from 8 to 40 (US population mean=20), where higher scores indicate worse sleep.<sup>29</sup>

**Insomnia Severity Index (ISI)**<sup>30</sup>. The ISI is widely used in sleep research and increasingly as a treatment response measure.<sup>31</sup> In this study, it was used as an indicator of subjective sleep quality. Participants rate their insomnia problems in the past 2 weeks on a 5-point scale. The seven items include the following examples: "difficulty falling asleep" (0=none - 4=very severe) and "how satisfied/dissatisfied are you with your current sleep pattern?" (very satisfied - very dissatisfied). A total score is derived by summing responses, ranging from 0-28 (0-7=absence of insomnia; 8-14=subthreshold insomnia symptoms; 15-21=clinical moderate severity insomnia; 22-28=clinical severe insomnia).

**WASO, SOL, and sleep efficiency.** Indices of these constructs were derived from the Sleep Timing Questionnaire (STQ).

#### Sleep quantity and timing

**STQ.** STQ<sup>32</sup> sleep quality, quantity, and timing and via questions about retrospective habitual bed and rising times. It provides information similar to that obtained using a prospective sleep diary. Participants report earliest, latest and usual "good

night" and "good morning" times before work/school days and days off. In addition, it asks participants to estimate usual bedtime and waketime stability, as well as usual SOL and WASO. STQ item 17 ("on most nights, how long does it take you to fall asleep on average?") and STQ item 18 ("on most nights, how much sleep do you lose, on average, from waking up during the night, e.g., to go to the bathroom?") were analyzed separately as indicators of the sleep quality variables, SOL and WASO, respectively.

STQ responses were used to create five subscales describing usual sleep (weighted 5 workdays to 2 days off). Sleep quantity was measured as the duration of time between usual sleep- and wake-times, less reported WASO and SOL. Sleep efficiency (a measure of quality) describes the percentage of reported time spent in bed (from bed- to waketime) estimated as asleep (duration/time in bed). Sleep timing was assessed by calculating usual bedtimes, waketimes, and sleep midpoint times from the STQ. Sleep/waketime and sleep midpoints obtained via sleep diary have been shown to be appropriate estimates of dim light melatonin onset and, in turn, circadian phase.<sup>33,34</sup>

#### Sleep-related daytime impairment

**Excessive daytime sleepiness (Epworth Sleepiness Scale [ESS]).** The ESS<sup>35</sup> is a widely used questionnaire designed to evaluate the level of habitual sleepiness (or sleep propensity) during the day. The scale comprises eight items that describe typical day-to-day situations (e.g., sitting and reading or watching television). Likely sleepiness in each situation, or imagined sleepiness in each situation, is reported. Each item can be rated from 0-3 points (0=would never doze, 3=high chance of dozing), with the final score ranging from 0 to 24. The proposed range for normal sleep propensity is 0-10.<sup>36</sup> The ESS has good reported internal consistency and reliability.<sup>37</sup>

**Sleep-related functional impairment (PROMIS) Sleep-Related Impairment - Short Form 8a; Version 1.0 (PROMIS8a)**<sup>25</sup>. The PROMIS8a is the second of the two short-form static



sleep measurement scales developed from the PROMIS item banks. PROMIS8a measures daytime impairment related to sleep.<sup>25,26</sup> PROMIS8a assesses perceived sleepiness and sleep-related impact on daytime functioning over the last 7 days. Responses are made on a 5-point scale ranging from 1 (not at all) to 5 (very much). An example item is: "I had a hard time getting things done because I was sleepy" and "I felt alert when I woke up." PROMIS8a is scored by reversing item 2 and summing items for a total score, which ranges from 8–40. The mean score for the US population is 16.<sup>38</sup>

### Procedure

Ethical clearance was provided by the university's Human Research Ethics Committee. Consenting participants completed a battery of measures, including the sleep measures. The core battery used block randomization: sleep measures were presented in a fixed order but were randomized with other dimensions of functioning. The questionnaires were administered online using Key Survey (WorldAPP, Version 8.2; 2013). Three items to test for indiscriminate responding were included.<sup>39</sup> To remain in the sample, participants were required to respond correctly to at least two of these items, and a further post-experimental check was used to verify that they understood and complied with the study instructions. Volunteers received bonus course credit if they were recruited from the undergraduate participant pool, or a chance to receive a randomly drawn prize valued at AU\$100.

### Results

Raw scores were analyzed using IBM Statistical Package for the Social Sciences, version 21. First, preliminary data cleaning and screening were conducted. A missing data analysis revealed minimal missing data on PROMIS8a, PROMIS8b, and ISI (0–2.9%), which was missing "completely at random," Little's MCAR,  $\chi^2(267) = 83.233, p = 1.00$ . Expectation-Maximization was used to impute missing values for these measures.<sup>40</sup> Missing values were not imputed when participants had not completed an entire scale or for the STQ because these data were coded as times (e.g., 7 AM or 7 PM). When data were missing for the STQ AM and PM values, these were logically derived (for example, a "9.30" bedtime was coded as PM). Three cases were excluded from STQ analyses because the missing data could not be logically derived (e.g., wake-times reported as an hour before bedtimes).

Relevant assumptions were checked to determine suitability of parametric analyses. Data were distributed normally unless otherwise stated. Three significant outliers were identified on the STQ SOL (one outlier) and STQ WASO (two outliers). These outliers were adjusted to the next highest value plus one, as per Field.<sup>41</sup> Data missing for a complete scale were deleted listwise. A significance level of 0.05 was used for analyses unless stated otherwise. Effect size was calculated using the Cohen *d*, and values were interpreted as per recommendations (i.e., 0.2 = small, 0.5 = medium, 0.8 = large).<sup>41,42</sup>

Descriptive statistics for sleep measures and group comparisons are shown in Table 3. To examine differences in sleep quality, quantity, timing, and daytime impairment, independent samples *t* tests were used for group comparisons (where parametric assumptions were breached, nonparametric equivalent tests were performed). mTBI vs. control and mTBI vs. CMC group comparisons revealed the same pattern of results in terms of statistical significance, with the exception that the sleep midpoint measure changed from nonsignificant to significant. For CMCs, effect sizes were slightly smaller for sleep quality and daytime impairment measures, but slightly larger for sleep timing measures (Table 3). This section describes the results from the mTBI vs. control comparisons only.

The mTBI vs. control group comparisons revealed statistically significant differences on three of the five sleep quality measures. The mTBI group self-reported poorer sleep quality in terms of sleep disturbance (PROMIS8b), WASO, and insomnia symptoms; however, there were no significant group differences for SOL or sleep efficiency. On the PROMIS8b, the control group closely approximated the US population mean of 20,<sup>43</sup> whereas the mTBI group scored higher than this, indicating poor sleep quality relative to this normative standard. Using the US population data as a cut point, 78.8% of the mTBI group scored greater than the US population mean on the PROMIS8b, while only 42.4% of the control group did so,  $\chi^2(1) = 9.14, p = 0.003$ .

mTBI participants also reported significantly more ISI insomnia symptoms than controls. Using the insomnia severity scoring guidelines, the percentage of participants meeting the cutoffs for the insomnia criteria was calculated. In the mTBI group, 25% had severe clinical insomnia, 46.9% had mild clinical insomnia, and the remaining 28.1% had subthreshold insomnia. In the control group, 9.1% had severe clinical insomnia, 21.2% had mild clinical insomnia, and 69.7% had subthreshold insomnia. The percentage of participants meeting these ISI criteria in the mTBI and control groups was significantly different,  $\chi^2(2) = 11.29, p = 0.001$ .

No differences were found between mTBI and control participants on measures of sleep quantity and timing. Measures of daytime impairment showed that mTBI participants reported increased sleep-related impairment on the PROMIS8a when compared with controls, but their level of daytime sleepiness as measured by the ESS was not significantly different from controls. Both the mTBI group and controls reported mean ESS scores higher than 10, suggesting they experienced clinically significant subjective sleepiness.<sup>44</sup>

### Discussion

This study sought to investigate whether persons who had sustained an mTBI between 1 and 6 months before study participation experienced more sleep disturbance than matched controls and describe the nature of this disturbance. Results revealed significant differences on aspects of sleep quality (on three of the five measures, medium to large effects) and sleep-related daytime impairment, but not on self-reported sleep duration or timing. These results appear robust given that the partial internal replication yielded very similar outcomes, albeit with smaller effects.

The finding of group differences in sleep quality, with the exception of SOL and sleep efficiency, is generally consistent with the literature. For example, the PROMIS8b result is consistent with studies that have shown a decrement in subjective sleep quality for patients with TBI using the PSQI.<sup>19,45,46</sup> This study is the first to find a sleep quality effect using the PROMIS8b, a measure that has been suggested for use in TBI research.<sup>28</sup>

This study found that the mTBI group's WASO was almost twice as long as that reported by controls. This quantitative estimate is consistent with previous research showing that mTBI participants report higher scores on the sleep disturbance subscale of the PSQI.<sup>19,45</sup> Perceived frequent nighttime awakenings were found to be the primary complaint in people with mTBI 6 weeks post-injury (35% of a sample of 443 mTBI participants complained of frequent awakenings).<sup>9</sup> Objective differences in WASO, however, have not been consistently demonstrated,<sup>19,45,47</sup> suggesting a need for further investigation, because the subjective experience of insomnia is central to its diagnosis.<sup>48</sup> Results from the ISI in this study indicate that higher distress because of poor sleep was experienced by the

TABLE 3. DESCRIPTIVE STATISTICS AND BETWEEN-GROUP COMPARISONS USING INDEPENDENT SAMPLES T TESTS ON FOUR FACETS OF SLEEP

Measure	1. Control (n = 33)			2. mTBI (n = 33)			3. CMC (n = 33)			I vs 2			2 vs 3					
	M	(SD)		M	(SD)		M	(SD)		t (df)	95% CI	p	d	t (df)	95% CI	p	d	
<b>Sleep quality</b>																		
PROMIS8b (disturbance)	20.01 (5.84)	25.49 (5.72)	21.26 (7.55)	-3.85 (64)	[-8.32, -2.63]	<.001	.96	-2.57 (59.59)	[-7.53, -0.94]	.007	-.64							
STQ SOL <sup>a</sup>	25.06 (17.09)	25.97 (15.68)	23.93 (18.52)	-0.45 (61)	[-9.16, 7.35]	.414	.05	-0.46 (59)	[-10.85, 6.78]	.323	-.12							
STQ WASO <sup>a</sup>	12.81 (18.56)	23.35 (24.23)	12.1 (17.13)	-1.94 (61)	[-21.39, 0.31]	.029	.50	-2.09 (59)	[-22.00, -0.51]	.021	-.54							
ISI <sup>a</sup>	13.42 (4.60)	17.53 (5.27)	15.09 (5.59)	-3.35 (63)	[-6.56, -1.66]	<.001	.84	-1.81 (63)	[-5.13, 0.25]	.038	-.46							
STQ Sleep Efficiency M <sub>%</sub> (SD)	92.14 (5.88)	89.59 (8.89)	92.45 (6.47)	1.30 (57)	[-0.01, .06]	.100	-.34	1.42 (57)	[-1.18, 6.91]	.081	.37							
<b>Sleep quantity</b>																		
STQ sleep duration: M <sub>hours</sub> (SD) <sup>b</sup>	7:56 (60 min)	7:32 (84 min)	7:48 (79 min)	1.28 (57)	[-0:13, 1:02]	.104	-.34	.75 (57)	[-0:26, 0:58]	.229	.20							
<b>Sleep timing</b>																		
STQ usual bedtime M <sub>Time</sub> (SD) <sup>a,c</sup>	23:01 (74 mins)	22:54 (70 mins)	23:25(84 mins)	0.36 (58)	[-0:30, 0:44]	.725	.09	1.54 (58)	[-9:32, 1:11]	.065	.40							
STQ usual waketime M <sub>Time</sub> (SD) <sup>a,c</sup>	07:40 (72 mins)	07:16 (76 mins)	07:50(82 mins)	1.21 (57)	[-0:15, 0:61]	.233	-0.32	1.62 (57)	[-8:07, 1:15]	.056	.43							
STQ sleep midpoint M <sub>Time</sub> (SD) <sup>a,c</sup>	03:20 (69 mins)	03:05 (65 mins)	03:38(76mins)	0.81 (57)	[-0:20, 0:49]	.422	.21	1.75 (57)	[-4:50, 1:09]	.043	.46							
<b>Sleep-related daytime impairment</b>																		
PROMIS8a (impairment) <sup>a</sup>	19.80 (7.68)	23.64 (6.22)	20.27 (7.00)	-2.21 (63)	[-7.31, 0.37]	.016	.56	-2.05 (63)	[-6.64, -0.08]	.023	.52							
Epworth Sleepiness Scale	14.12 (4.50)	14.69 (4.82)	14.24 (3.06)	-0.490 (63)	[-2.88, 1.74]	.313	.12	-0.45 (52.68)	[-2.49, 1.58]	.330	.11							

N = 69.

SD, standard deviation; mTBI, mild traumatic brain injury; CMC, close-matched control; CI, confidence interval of the mean difference; d, Cohen's d for independent samples; PROMIS8b (disturbance) = Patient-Reported Outcomes Information System Sleep Disturbance Version 1.0 Short Form; STQ, Sleep Timing Questionnaire; SOL, sleep onset latency (from the STQ); WASO, wake after sleep onset (from the STQ); ISI, Insomnia Severity Index; PROMIS8a (impairment) = Patient-Reported Outcomes Information System Sleep-Related Impairment Version 1.0 Short Form.

<sup>a</sup>Nonparametric Mann-Whitney U tests were conducted for these variables; however, the results did not change. Therefore, the t test that is reported here is for consistency.

<sup>b</sup>Mean hours and minutes sleeping (e.g., 7:56=7h and 56 min).

<sup>c</sup>Clock hour, in hours and minutes.

mTBI participants compared with controls; on average, the mTBI group reported clinically significant moderate insomnia whereas controls reported subthreshold insomnia.<sup>30</sup>

The SOL result was inconsistent with the findings from previous studies; it was not different for mTBI participants and controls. This result was surprising considering that the mTBI group reported greater insomnia severity on the ISI. Both groups in the current study, however, reported a relatively long average SOL of 35 min (>20 min is considered long).<sup>49</sup> The absence of a group effect on SOL may be attributable to the large proportion of university students in the sample, a population for which there is a higher probability of sleep dissatisfaction, insufficient sleep, and irregular sleep-wake patterns.<sup>50</sup> It is possible that group differences on this variable were obscured by a ceiling effect that might not be observed in other populations. The final measure of sleep quality, sleep efficiency, revealed no significant group difference, which may be a result of the similarly high SOL in both groups.

In terms of sleep quantity, this study found no differences in sleep duration between the mTBI group and controls. Moderate-to-severe TBI appears to be a risk factor in developing hypersomnia,<sup>11</sup> and when differences in sleep duration have been found previously compared with controls, this has usually involved mixed severity TBI rather than an mTBI only sample. One previous study found that persons with mTBI had shorter sleep duration than controls<sup>47</sup>; however, these patients were assessed after presentation for sleep complaints.

This study predicted no differences in sleep timing between the groups, and the study results supported this hypothesis. This result is generally consistent with past findings.<sup>9,51</sup> A contrary result, however, was reported by Ayalon and coworkers<sup>52</sup> Their group found that 36% of a selected sample of 42 mTBI participants who complained of insomnia in fact had a circadian rhythm disorder. When we compared the mTBI group against CMCs, the measure of sleep midpoint was significantly earlier for the mTBI group than the CMCs, perhaps suggesting a trend toward a phase advanced circadian rhythm. Overall, however, the findings from the present study suggest that disturbances of the timing and circadian regulation of sleep may not be as prominent in unselected mTBI samples.

mTBI participants reported greater daytime sleep-related impairment but did not differ significantly with regard to their daytime sleepiness in comparison with controls. Both groups reported greater sleep-related impairment on the PROMIS8a than the US population mean<sup>38</sup>; Australian normative data for this test were not available. There were no differences between mTBI participants and controls on daytime sleepiness, although both groups reported significant levels of daytime sleepiness. Excessive daytime sleepiness is experienced as an inability to maintain the desired level of alertness or to fall asleep at times when doing so would be unwanted.<sup>2</sup>

A previous study by Gosselin and colleagues<sup>19</sup> did not find an effect of mTBI on excessive daytime sleepiness, but an effect has been reported using an objective measure, the Maintenance of Wakefulness Test.<sup>47</sup> Assessment of sleep-related daytime impairment in patients with mTBI warrants further investigation, as the effects of sleep on everyday functioning may be greater after mTBI if a quick return to usual levels of functioning is expected.

Previous research has been difficult to interpret because of differences related to characterization of mTBI (e.g., injury severity, time since injury, definition of mTBI, inclusion criteria, use of controls), and sleep (e.g., nature, severity, method of measurement). This study has highlighted the need for more well-controlled studies of this issue. Our approach may stimulate further thinking about the way sleep, or its facets, feature in mTBI outcome. In this

study, the exclusion of persons with comorbid disorders could suggest that sleep disturbance (i.e., reduced sleep quality) occurs independently of other factors that contribute to post-injury outcome, although we did not exclude all possible comorbidities and there were group differences on sleep disturbance because of pain. It should also be noted that the participants were probably not significantly functionally impaired and the findings may not generalize to a more impaired group, or to a group with the comorbidities that we excluded.

This study has several limitations. This study did not include objective sleep measures, and it is unclear whether similar results would be obtained with such measures. This study used a predominantly student sample, and findings may not generalize to samples with low (<12 years) levels of education or samples with different daily routines/sleep patterns. The group differences could be interpreted as caused by sleep-disrupting pain, because the groups were not matched on the number of nights of sleep disturbed by pain. A replication of this study with a no/low pain-related sleep disturbed mTBI group is recommended.

The time since injury, while controlled, breached some definitions of chronicity (e.g., symptoms persisting beyond 1 month may indicate post-concussional syndrome according to the World Health Organization,<sup>53</sup> whereas symptoms persisting beyond 3 months are required by the American Psychiatric Association, fourth edition, criteria).<sup>54</sup> This study did not use a longitudinal study design to track change over time, and causation between injury and sleep complaint should not be inferred. We were unable to verify the mTBI participants' injury and as such had limited detail on the nature of the mTBI (e.g., Glasgow Coma Scale score); however, participants self-reported mTBI was based on a clear operational definition of mTBI.<sup>15</sup>

The results provide no information on the presence or nature of sleep disorders that require objective measurement for diagnosis (e.g., obstructive sleep apnea), and the findings may not be specific to sleep quality or daytime sleepiness; rather, they may represent a general "complaint" tendency. A study of the group effect on objective sleep measures is recommended and could yield additional information about sleep changes after mTBI that may be expected. At the individual level, such data could be used as part of a therapeutic process to further understand the complaint. This process should also include considering if a formal diagnosis of the sleep complaint is warranted (or if referral to a sleep specialist is needed), and exploration of the causal attribution that mTBI patients may have of their sleep complaint.

This study has revealed the importance of detailed sleep assessment in patients after mTBI. If assessed by a single item, depending on the sleep facet tested, different conclusions might have emerged (ranging from no group differences to group differences). In this study, multiple indices of sleep were used to yield a comprehensive questionnaire-based sleep assessment. As argued by Iverson and associates<sup>55</sup> and others,<sup>56</sup> and in light of the complex array of factors that contribute to poor outcome from TBI,<sup>57</sup> recovery may be improved by focusing on treatable aspects of the injury response. Sleep disturbance may be treatable, even when comorbid with TBI,<sup>2,7</sup> but the nature of clinical disturbance must first be carefully established.

There is limited literature assessing treatment approaches in this population.<sup>10</sup> This study's findings suggest that some sleep therapies (e.g., bright light therapy, melatonin, both of which are targeted at circadian dysfunction) may be of limited use after mTBI. Psychological and behavioral therapies such as cognitive behavioral therapy for insomnia (CBTi), however, which is the first-line therapy recommended for insomnia, may be beneficial.<sup>58</sup>

CBTi has demonstrated efficacy for the treatment of insomnia even in the presence of significant comorbid psychopathology. Concurrent CBTi treatment has the potential to improve outcomes both for sleep and comorbid conditions, suggesting that in conditions that involve sleep disruption (such as pain), treatment plans with a specific sleep component are likely to improve overall outcome.<sup>59</sup> CBTi has been successfully implemented in a mixed severity TBI sample, with improvements similar to those seen in other populations, and benefits sustained at 3 months follow-up.<sup>60</sup> Even for subclinical sleep disturbance, clinicians are urged to facilitate access to wellness programs to optimize sleep after TBI,<sup>61</sup> and in the acute period (days post-injury) rest is recommended.<sup>62</sup> A randomized controlled trial to test the efficacy of such interventions in mTBI patients is encouraged.

Together these findings suggest that after 1 to 6 months post-mTBI, reduced sleep quality and sleep-related impairment are the most likely sleep complaints. After mTBI, longer nighttime awakenings are reported, and insomnia symptoms may be worse. Irrespective of their cause, these features need to be addressed in recovery. Future research should examine the association between sleep disturbance and mTBI prospectively and use objective measures to gain a broader understanding of this problem.

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