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Original Article

Evidence of actigraphic and subjective sleep disruption following mild traumatic brain injury

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ABSTRACT

Objective/background: Mild traumatic brain injuries (mTBI) are frequently associated with long-term, self-reported sleep disruption. Objective corroboration of these self-reports is sparse and limited by small sample sizes. The purpose of this study was to report on actigraphically-measured sleep outcomes in individuals with and without a history of recent mTBI in two U.S. cities (Boston, MA and Tucson, AZ).
Patients/methods: Fifty-eight individuals with a recent (within 18 months) mTBI and 35 individuals with no prior mTBI history were recruited for one of four studies across two sites. Participants completed a minimum of one week of actigraphy. Additionally, mTBI participants self-reported daytime sleepiness, sleep disruption, and functional sleep-related outcomes.
Results: In Boston, mTBI participants obtained less average sleep with shorter sleep onset latencies (SOL) than healthy individuals. In Tucson, mTBI participants had greater SOL and less night-to-night SOL variability compared to healthy individuals. Across mTBI participants, SOL was shorter and night-to-night SOL variability was greater in Boston than Tucson. Sleep efficiency (SE) variability was greater in Tucson than Boston across both groups. Only SOL variability was significantly associated with daytime sleepiness ($r = 0.274$) in the mTBI group after controlling for location.
Conclusion: Sleep quality, SOL and SE variability, are likely affected by mTBIs. Between-group differences in each site existed but went in opposite directions. These findings suggest the possibility of multiple, rather than a singular, profiles of sleep disruption following mTBI. Precision medicine models are warranted to determine whether multiple sleep disruption profiles do indeed exist following mTBI and the predisposing conditions that contribute to an individual's experience of sleep disruption.

1. Introduction

Each year, at least 1.5 million documented and undocumented mild traumatic brain injuries (mTBIs) occur in the United States each year [1,2]. mTBIs are the result of external forces to the head or body resulting in the disruption of normal brain function, with or without short-term loss of consciousness, and the absence of gross abnormalities on conventional diagnostic neuroimaging [3,4]. These injuries result in a wide range of somatic symptoms, as well as changes and impairments in cognitive, motor, and behavioral functioning [3,5,6]. Some of these changes appear to be transient, naturally recovering to preinjury levels within one–three months [5,7–9]. However, many others (eg, depression, pain, increased daytime fatigue, and poor sleep) may have long-term sequelae that do not resolve without intervention [10–15].

Post-mTBI sleep changes are a common complaint, with 30–70% of individuals reporting some form of sleep disruption [10,16]. The most frequent of these complaints are self-reported sleep disruption, insomnia, and daytime sleepiness or fatigue [15,17–22]. However, these self-reports are generally not corroborated by objective findings [11,23–25]. Objective findings of sleep disruption specific to mTBI are limited. Several studies employing polysomnography have demonstrated that individuals with a history of mTBI get poorer sleep (lower sleep efficiency, more frequent and longer nocturnal wakefulness) and have higher overall physiological arousal compared to either population norms or control participants [26–29]. However, these findings are inconsistent [11,24,30,31] and a recent meta-analysis suggests that such findings may not persist into the chronic phase (>6 months post-injury) [32].

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Additional studies employing actigraphy have corroborated findings of lower sleep efficiency and increased nighttime awakenings [33–35]. Actigraphy-based studies have further identified circadian rhythm sleep disorders following mTBI [36], as well as findings indicating that total 24-hour sleep time may be greater in individuals immediately after a mTBI, and that this recovers over time [33,34]. However, these findings are also not consistently observed [37,38], and higher intra-individual variability following mTBI than in controls may partially explain inconsistent findings across both PSG and actigraphy studies [34,37].

Two major challenges in post-mTBI sleep-related research are overall small sample sizes and the reliance on mixed severity TBI samples [39]. Consequently, the findings across the literature require further corroboration and exploration in order to more completely describe the generalizability. The purpose of this study was to compare individuals with a recent mTBI (<18 months prior) to healthy controls with no prior history of mTBI on seven days of at-home actigraphy. We hypothesized that both sleep quantity and sleep quality (eg, greater nighttime awakening, lower sleep efficiency) would be worse in those with a recent mTBI. We additionally hypothesized that post-mTBI individuals would exhibit greater night-to-night variability in these actigraphy-based sleep metrics than controls.

2. Material and methods

Study procedures were evaluated and approved by the Institutional Review Boards of Partners Healthcare, the University of Arizona College of Medicine, and the U.S. Army's Human Research Protections Office. All participants provided written informed consent prior to participation.

2.1. Participants

Data for the present study were acquired from four samples of individuals enrolled in four separate studies that employed similar methodology for recruitment and collection of actigraphy. Two of these studies were completed in Boston, MA and two are on-going in Tucson, AZ. Participant demographics are summarized in Table 1.

2.1.1. Mild traumatic brain injury participants

A total of 58 individuals with a recent mTBI (time since injury: 8 ± 4.74 months; male/female: 23/35) were recruited from the greater Boston ($n = 28$) and Tucson ($n = 29$) areas. In both locations, individuals were recruited via community fliering and were required to provide documentation indicating either direct observation of the injury and immediate sequalae (eg, by a coach) or the diagnosis of a concussion by a qualified professional (eg, physician, athletic trainer). For both locations, mild traumatic brain injury was defined according to criteria consistent with the American Congress of Rehabilitation Medicine [40] and VA/DoD Guidelines [41]. Specifically, a mTBI was defined as a physiological disruption of brain function caused by a traumatic injury to the head, resulting in a Glasgow Coma Scale (if obtained) between 13 and 15 within 24 h of injury, loss of consciousness lasting no more than 30 min, posttraumatic amnesia lasting less than 24 h, altered mental state lasting less than 24 h, and/or focal neurological damage that may be transient [40,41]. Unrelated neuroimaging findings from these samples have been reported elsewhere [42,43] but the use of actigraphy in the present paper is novel and has not been previously published.

2.1.2. Healthy controls

Sleep-related data were additionally available from two separate groups of healthy control participants. Twenty-four individuals were recruited in Boston. These healthy controls met the following criteria: no history of psychological, neurological, sleep, or other medical disorders; self-reported sleep duration within the top or bottom quartile of the population; no history of head injury with loss of consciousness or post-traumatic amnesia; daily caffeine intake less than 300 mg per day; no drug or alcohol abuse in the past six months; no history of smoking; no use of medications with drowsiness as a side effect; and not pregnant. Unrelated results from the primary study for these participants have previously been published [44] or are currently under review. However, their use in this study provides novel insights.

An additional 11 healthy individuals were recruited in Tucson. These healthy controls met the following criteria: no history of psychological, neurological, sleep, or other medical disorders; no history of concussion or TBI; no history of cardiac conditions; no presence of excessive daytime sleepiness; no presence of irregular circadian schedule (eg, shift work); daily caffeine intake less than 300 mg per day; no current use of medications (except birth control), recreational drugs, or tobacco; and not pregnant.

2.2. Actigraphy

All participants completed a minimum seven days of actigraphy using either a Philips Respironics Actiwatch Spectrum (mTBI groups) or the Philips Respironics Actiwatch-2 (healthy control groups). Data for the Tucson mTBI and healthy controls groups were collected using 1 min epochs. Data for the Boston mTBI group was collected using 2 min epochs.

Actigraphy data were processed in the Philips Actiware 6 software. All data were scored automatically in the software using the default scoring algorithm, with sleep time scored based on minutes of immobility. The algorithm analysis criteria were set as follows for all subjects: wake threshold value of 40 activity counts, 10 immobile minutes for sleep onset and sleep end; white light threshold of 1000 lux. Automatic scoring was visually inspected by a trained technician and scores were modified as needed based on sleep diary data to reconcile unclear recordings. Sleep onset latency (SOL), wake after sleep onset (WASO), sleep efficiency (total sleep time/total time-in-bed; SE), and total nighttime sleep duration were extracted. The coefficient of variation (standard deviation/mean; CV) as a measure of intra-individual variation for each individual was calculated for each measure.

2.3. Self-reported outcomes

Participants in each of the parent studies completed comprehensive battery of neuropsychological exams and self-reported questionnaires. Here we report the outcomes from three of these self-report questionnaires only.

2.3.1. The Epworth Sleepiness Scale (ESS)

All participants completed the ESS, a self-report measure of daytime sleepiness [45]. Scores range from 0 to 24 and a cutoff score of 10 has been identified to indicate excessive daytime sleepiness [46].

2.3.2. The Pittsburgh Sleep Quality Index (PSQI)

Participants in the mTBI groups completed the PSQI, a self-report measure regarding overall sleep quality [47]. Lower scores indicate better sleep quality. Total scores greater than 5 indicate poor sleep in the general public [47], although scores greater than 8 have been identified as more sensitive in TBI samples [48]. The PSQI has both good test-retest reliability ($r > 0.80$) [47] and post-mTBI sleep disruption sensitivity [15,49].

Table 1
Demographic characteristics, self-reported outcomes, and actigraphy measures by site and group.

	Boston		Tucson	
	HC	mTBI	HC	mTBI
N	24	28	11	29
Age (years)	25.8 ± 5.33	22.8 ± 7.16	19.9 ± 1.51[a***]	26 ± 8.22[b***]
Sex (M/F)	10/14	13/15	3/8	10/19
BMI (kg/m^2)	24.0 ± 3.72	25.4 ± 3.67	21.8 ± 3.66[a]	25.4 ± 6.26[b*]
Months post-injury		6.77 ± 3.97		9.21 ± 5.30
Mechanism of Injury (n)				
SRC[c]	–	17	–	7
MVA	–	5	–	13
Environmental[d]	–	4	–	4
Bicycle	–	1	–	2
Violence[e]	–	1	–	3
Participation month (n)				
January	2	1		1
February	4	4	3	1
March	4	6	6	2
April	1		2	3
May				1
June	1	6		4
July		3		3
August	1	1		1
September	1	2		7
October	4	2		2
November	5	2		2
December	1	1		2
Self-report measures				
ESS Score	5.92 ± 3.82	10.2 ± 3.19[f***]	5.55 ± 3.39	8.62 ± 3.24[b*]
PSQI Total Score	–	7.14 ± 2.27	–	7.76 ± 3.24
FOSQ Total Score	–	16.47 ± 1.95	–	15.90 ± 3.34
Actigraphy measures				
Sleep duration				
Mean (min)	439.98 ± 38.99	407.51 ± 59.64	405.30 ± 68.59	425.55 ± 53.01
CV	0.16 ± 0.07	0.18 ± 0.08	0.17 ± 0.07	0.18 ± 0.08
SOL				
Mean (min)	8.98 ± 5.59	3.43 ± 2.53	10.13 ± 9.17	20.66 ± 14.27
CV	1.17 ± 0.39	1.40 ± 0.56	1.40 ± 0.44	1.04 ± 0.52
WASO				
Mean (min)	52.23 ± 17.64	56.39 ± 29.60	62.05 ± 37.18	52.36 ± 19.01
CV	0.39 ± 0.16	0.44 ± 0.24	0.43 ± 0.24	0.43 ± 0.37
SE				
Mean (%)	85.31 ± 3.78	85.94 ± 6.43	82.21 ± 7.93	82.24 ± 5.34
CV	0.06 ± 0.03	0.05 ± 0.04	0.09 ± 0.08	0.08 ± 0.04

Note. Values are provided as mean ± SD unless otherwise indicated. Two sample *t*-tests were used to identify significant differences between groups for continuous variables. PSQI and FOSQ outcomes were not recorded for the healthy control participants in Boston or Tucson. HC: Healthy Control; mTBI: Mild Traumatic Brain Injury; BMI: Body Mass Index; SRC: Sports-related concussion; MVA: Motor vehicle accident; ESS: Epworth Sleepiness Scale; PSQI: Pittsburgh Sleep Quality Index; FOSQ: Functional Outcomes of Sleep Questionnaire; CV: Coefficient of Variation; SOL: Sleep Onset Latency; WASO: Wake After Sleep Onset; SE: Sleep Efficiency.
*: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$.
[a] Boston vs. Tucson HC.
[b] Tucson mTBI vs HC.
[c] Includes competitive and recreational (ie $n = 1$ boating accident) sports.
[d] Includes contact with the environment due to slipping/tripping, alcohol-related mTBI, and falling objects.
[e] Includes interpersonal violence and animal attacks.
[f] Boston mTBI vs HC.

2.3.3. The Functional Outcomes of Sleep Questionnaire (FOSQ)

The FOSQ is a self-report questionnaire designed to identify the impact of sleep, particularly excessive daytime sleepiness on activities of daily living [50]. Scores on the FOSQ range from 5 to 20, and higher scores are better (greater overall function) [51].

2.4. Statistical analyses

All statistical analyses were conducted in R (including the tidyverse [52–54], lmerTest [55], and rsq [56] packages) with *a priori* significance set at $p < 0.05$. Group differences in demographic and personal characteristics were computed using two-sample *t*-tests a χ^2 tests as appropriate. To identify differences in sleep measures over the seven days of actigraphy, we fit individual linear mixed effects models using the lmerTest package. Main effects included mTBI group (healthy vs. mTBI) and location (Boston vs. Tucson) as well as the interaction term. These models utilized all available days of actigraphy for each individual, as between-group differences in weekly means may be obscured by high intra-individual variability [28,34,37]. Planned post-hoc comparisons were made within site (eg, healthy vs. mTBI in Boston) and within group (eg, Boston vs. Tucson mTBI) but not fully crossed (eg, not Boston healthy vs. Tucson mTBI). We also computed group x location ANOVAs on the CV data to identify intra-individual variability differences. We further report Cohen's d as a measure of effect size for reported post-hoc comparisons. For the linear mixed models, these effect sizes were computed on the estimated marginal means after adjusting for the random effects in the models, We additionally performed exploratory analyses within the mTBI participant group to evaluate the relationship between sleep and

self-reported outcomes. First, to assess whether sleep parameters improve over time since injury, we fit a linear model to the weekly mean and CV data with months since injury as the independent variable and controlled for location. We also fit individual linear models to the ESS, PSQI, and FOSQ scores with mean and CV data from the preceding week while controlling for location. These models allowed us to determine the extent to which prior sleep predicts self-reported sleep quality and sleep-related outcomes.

3. Results

3.1. Demographic data

Demographic and self-report outcomes are presented in Table 1. Healthy controls in Tucson were significantly younger than both the Boston healthy controls and Tucson mTBI participants. ESS total scores were higher in the mTBI groups than the matched controls in each respective location.

3.2. Linear mixed effects models of actigraphy

3.2.1. Total nighttime sleep

Post-hoc analyses revealed that healthy control participants in Boston slept approximately 30 min more on average per night than both mTBI participants in Boston ($t = 2.716$, $p = 0.007$, $d = 0.76$; Fig. 1A) and healthy controls in Tucson ($t = 1.915$, $p = 0.056$, $d = 0.70$).

3.2.2. Sleep quality measures

SOL data required transformation [$(y = \ln(x + 1))$] prior to model fitting in order to reduce positive skewness in the residuals. SOL was shorter for the Boston mTBI subgroup than for the Boston healthy controls ($t = 5.060$, $p < 0.0001$, $d = 1.41$; Fig. 1B) and Tucson mTBI participants ($t = 8.275$, $p < 0.0001$, $d = 2.28$). Additionally, SOL was longer in the Tucson mTBI subgroup than the Tucson healthy controls ($t = 4.238$, $p < 0.0001$, $d = 1.5$).

Nightly WASO data required fourth root transformation to reduce positive skewness in the residuals. No statistically significant differences were observed for any post-hoc comparisons (Fig. 1C).

Sleep efficiency data required fourth power transformation to reduce negative skewness in the residuals. Post-hoc analyses demonstrated greater SE for mTBI participants in Boston compared to those in Arizona ($t = 3.428$, $p = 0.001$, $d = 0.91$) as well as healthy controls in Boston ($t = 2.568$, $p = 0.01$, $d = 0.71$).

3.3. Intra-individual variability

All CV data required log transformation prior to model fitting to address non-normality in the residuals. mTBI participants in Tucson had less variable SOL ($t = 3.137$, $p = 0.002$, $d = 0.83$; Fig. 2B) and more variable SE ($t = 2.866$, $p = 0.005$, $d = 0.76$; Fig. 2D) than mTBI participants in Boston. Additionally, Tucson mTBI participants had less variable SE than the Tucson healthy controls ($t = 2.616$, $p = 0.011$, $d = 0.93$; Fig. 2D). Finally, overall SE variability was greater in Tucson than Boston ($t = 2.628$, $p = 0.010$, $d = 0.55$; Fig. 2D) No other statistically significant pairwise comparisons were observed (Fig. 2A–D).

3.4. Relationship between actigraphy and self-reported outcomes

After controlling for location, SOL coefficient of variation significantly predicted ESS (Fig. 3). No other sleep measures were related to time since injury or self-reported outcomes.

4. Discussion

The purpose of this study was to identify differences in actigraphically-measured sleep characteristics between individuals with and without a history of mild traumatic brain injury. We hypothesized that individuals with a recent mTBI would have greater nighttime sleep duration and worse sleep quality, as well as greater night-to-night variability, than healthy controls, regardless of data collection location. These hypotheses were partially confirmed.

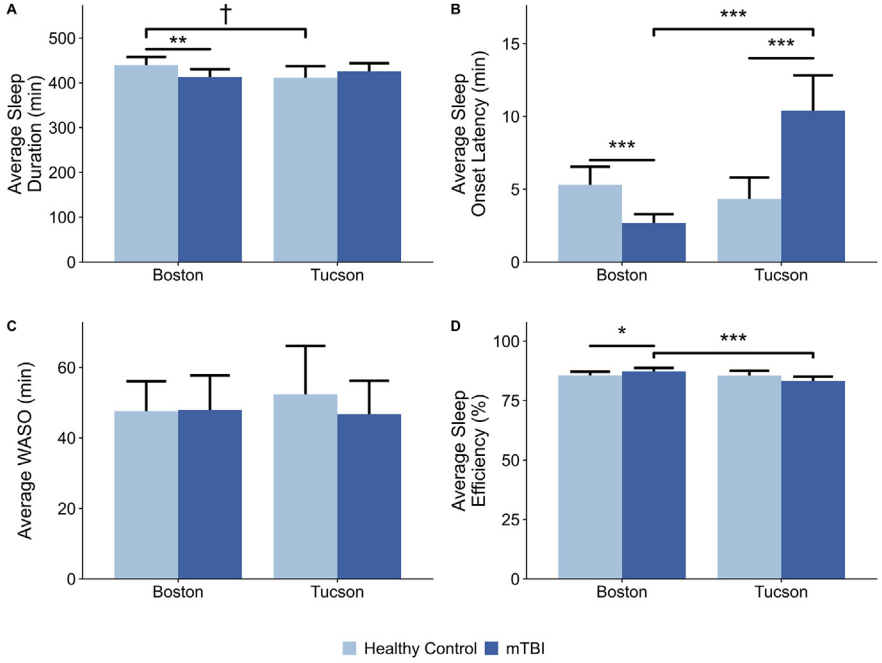

Fig. 1. Mean values for actigraphically-measured sleep variables by location (Boston, MA and Tucson, AZ) and group (healthy control or mild traumatic brain injury (mTBI)). Bars are presented as estimated marginal means ± standard error based on the linear mixed models. †: $p < 0.1$; *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$.

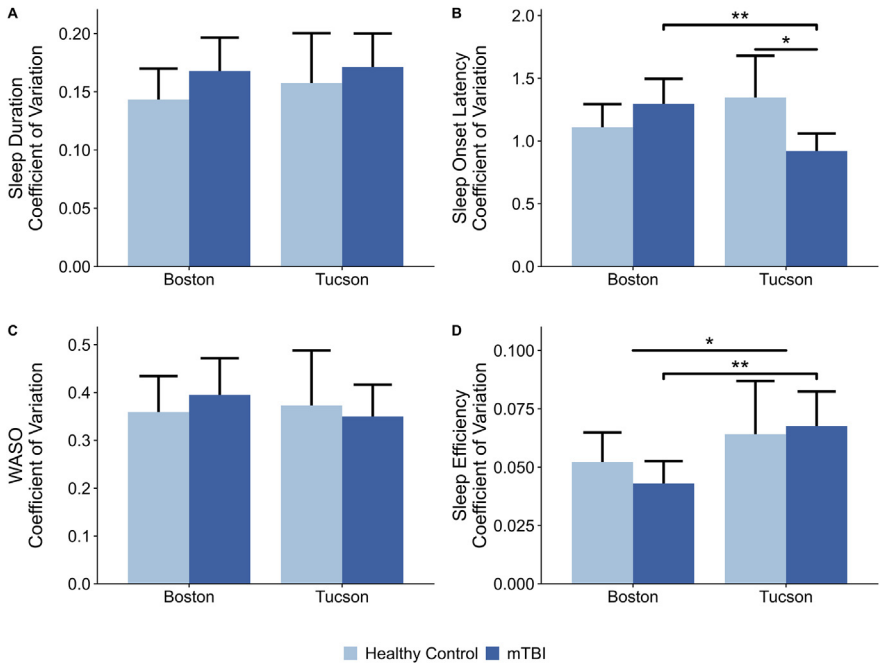

Fig. 2. Coefficient of variation (CV) for actigraphically-measured sleep variables by location (Boston, MA and Tucson, AZ) and group (healthy control or mild traumatic brain injury (mTBI)). Bars are presented as estimated marginal means ± standard error based on the linear mixed models. †: p < 0.1; *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$.

4.1. Objective sleep findings

Our initial hypotheses concerned the differences between healthy individuals and mTBI participants. Given the multi-site nature of our data, we included location in the models to address potentially systematic between-site differences. While not hypothesized, we found differing patterns of actigraphic sleep outcomes between the two sites. Individuals in the Boston mTBI group obtained, on average, 32 fewer minutes of sleep per night than their location-matched healthy controls. By contrast, the Tucson mTBI participants slept approximately 18 min longer per night than their location-matched healthy controls, though this finding was not statistically significant. Notably, the healthy controls in Tucson slept approximately 32 min less than the Boston healthy control group, putting them at a similar level as the Boston mTBI group. Thus, no consistent pattern of findings was observed for total sleep time

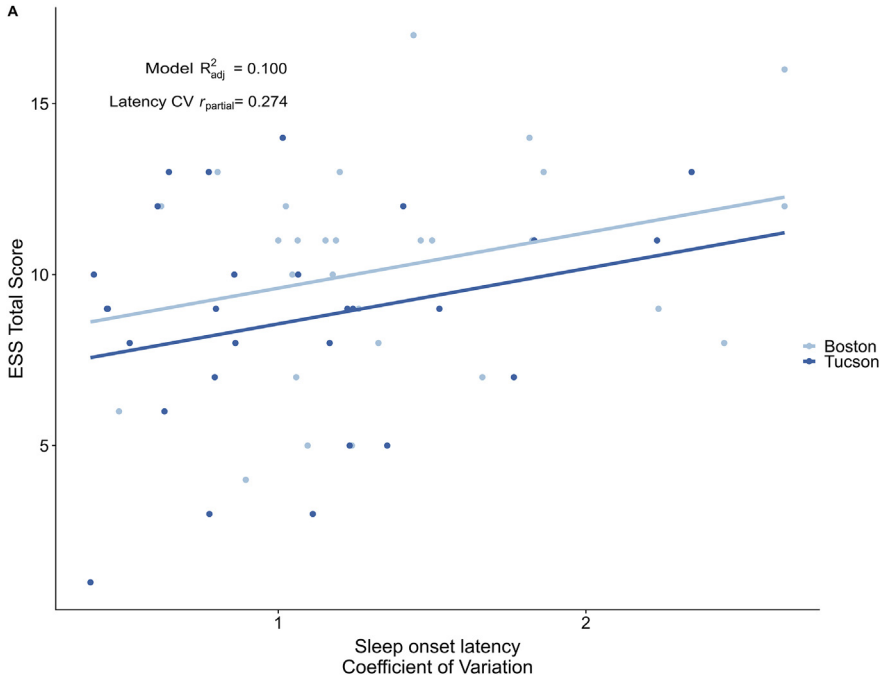

Fig. 3. Relationship between sleep onset latency coefficient of variation (CV) and daytime sleepiness scores (Epworth Sleepiness Scale; ESS). A significant positive association between increased sleep onset latency intra-individual variability and self-reported daytime sleepiness was observed in both sites. No between site differences were observed.

between those with a prior mTBI and healthy controls, although this may have been obscured by the between-location variability.

We observed similarly conflicting within and cross-location findings for average SOL (longer for mTBI in Tucson; shorter for mTBI in Boston), as well as intra-individual variability in SOL (more for mTBI in Boston; less for mTBI in Tucson). Collectively, average SE was lower in Tucson than in Boston while intra-individual variability was higher. However, there were no between group (mTBI vs. control) differences.

4.1.1. Potentially multiple profiles of post-mTBI sleep disturbance

Taken individually, the findings from the Boston subgroups showing reduced sleep in the mTBI sample would stand in opposition to other actigraphy-based studies indicating no differences or greater sleep duration in those with mTBI compared to population norms or controls [23,33,34,37]. However, the Tucson sub-samples would seem to confirm the no difference findings [37,38]. Additionally, no between-group differences were observed in night-to-night sleep duration variability, in contrast to prior findings [37]. Similarly, prior work generally reports no differences in actigraphically-measured SOL following mTBI [25,38,57], although one report suggests SOL may be decreased [33]. Our present findings suggest that SOL may be affected after mTBI, though the direction is unclear.

Taken together with the inconsistently reported effects of mTBI on sleep across the literature, these seemingly conflicting findings yield a critical observation on post-mTBI sleep. To date, studies in this area have employed small sample sizes from a single location and may or may not include a control group. As evident in the patterns of differences between healthy individuals and mTBI participants across the two sites, as well as the differences between the two groups of mTBI participants reported here; it is likely that, similar to the heterogeneity of mTBI mechanisms and individual responses to injury [6,58,59], self-reported and actigraphic sleep findings are highly individualized. Recent reports highlight the fact that there are multiple divergent clinical profiles of mTBI (ie, cognitive fatigue; oculomotor) [6,60–63]. Sleep disruption of all kinds, however, is considered a sub-component modifier of these clinical profiles, but not in itself a primary profile.

The findings in the present study suggest that there may likewise be multiple profiles of sleep disruption (eg, long latency vs. short latency; increased night-to-night variability vs. no change in variability; shorter sleep duration vs. unaffected sleep duration but longer onset latency). In light of the individually small sample sizes in each of our groups, this explanation is speculative at present. However multiple sleep disruption profiles, rather than a one-size-fits-all approach, are consistent with emerging clinical views of mTBI and would explain the inconsistent findings resulting from single, small cohorts of individuals following injury. The possibility of multiple sleep outcome profiles following mTBI merits further investigation with larger samples of not only individuals following mTBI but also reference cohorts.

4.1.2. Additional explanations for the observed patterns of responses

There are several other possible explanations for the pattern of findings in the present study. As stated previously, there are multiple mTBI clinical profiles [6,60–63]. Given the various mechanisms of injury leading to the most recent mTBI in the present participants, the clinical profiles in the present study may have varied significantly. We were unable to retrospectively create these profiles for our mTBI participants. As the relationship between current views of clinical profiles and sleep is unknown, there may be sleep effects driven by differences in injury mechanism and potentially varied clinical presentations leading to inconsistent between- and within-group findings. Particularly, the between-site differences in SE and SOL for the mTBI participants.

Second, a recent meta-analysis of sleep architecture in chronic (>6 months) TBI identified no overall differences in sleep architecture (measured via PSG) for those with mTBI compared to control participants. The authors, however, suggest caution when interpreting these findings in light of several limitations including inconsistent definitions of mTBI and the possibility that injury-related changes may resolve within six months [32]. Thus our inconsistent pattern of findings may be driven by the varied time since injury for our participants. However, we find this explanation unlikely because of (A) the lack of relationship between time since injury (in months) and any of the reported measures, even after accounting for location differences; and (B) post-hoc assessments of our models including time since injury as a covariate did not significantly improve the fits of any of our models.

Finally, in light of the between-site differences, particularly in both average SE and intra-individual variability, it is possible that location matters when interpreting actigraphy results. Prior work has shown that perceptions of sleep quality differ by geographic region [64,65]. Furthermore, sleep-related circadian rhythms are influenced by the amount of exposure to blue wavelength light, of which sunlight is a major contributor [66,67]. Given the seasonal differences between Boston and Tucson (eg, year-round availability of sunlight in Tucson) as well as a difference of just over 10° in latitude, the amount of daily light exposure may have differed significantly across sites and between individuals. Consequently, geographic and seasonal variation in sunlight exposure may exert influences on sleep timing, quantity, and quality that affect the findings of individual studies [68,69]. However, the implications of strictly geographic and seasonal influences on the outcomes reported here are not identified or well-supported by any extant literature and therefore require further exploration.

Regardless, this is the first multi-site mTBI-specific analysis of actigraphically-measured sleep with location-matched controls of which we are aware. Further work using tightly controlled geographic and season-matched samples is needed to identify the extent to which geographic location and seasonal variation may impact sleep-related outcomes.

4.2. Relationship between subjective and objective findings

An additional important finding from the present study is the further corroboration of prior studies identifying a discrepancy between perceived and objective sleep quality following mTBI. Across both mTBI groups, 50.9% ($n = 29/57$) of participants reported excessive daytime sleepiness (ESS score $\geq$ 10), 84.2% ($n = 48/57$) reported clinically significant PSQI total scores $\geq$ 5,[47] and 47.4% ($n = 27/57$) reported PSQI scores $\geq$ 8 [48]. Collectively, these self-reports indicate a high prevalence of perceived sleep disruption and daytime sleepiness in the mTBI group. However, only intra-individual variability in SOL significantly predicted ESS total scores. Higher variability in SOL was associated with greater daytime sleepiness, though the model including CV and location explained very little overall variance in ESS scores ($R^2 = 0.1$). Thus, individuals perceive poorer sleep and greater daytime fatigue, despite no relationship between objective and subjective measures. As previous authors have suggested, it may be that these objective and subjective measures are capturing differing aspects of the sequelae of post-mTBI recovery, and therefore provide complementary rather than conflicting outcomes [23].

4.3. Limitations

The findings from this study should be interpreted in light of several limitations. First, the participants in all of our groups were

recruited for different studies, each with individually small sample sizes. This is particularly true of the Tucson healthy control group ($n = 11$). Consequently, these findings should be conservatively viewed as preliminary results that require further corroboration.

Second, as noted previously, geographic and seasonal, as well as genetic, sociodemographic, and cross-cultural effects on actigraphically-quantified sleep remain largely unclear and, with the exception of geographic location, were not accounted for in these analyses. While the month (as a proxy for season) of participation is available, there were too few individuals at any given time point to adequately model the across-season variability. Future work should address these considerations in larger multi-site samples with seasonally-matched controls.

Third, the four samples reported here were recruited for four different studies with varied methods and goals. Consequently, there were between-sample differences in the actigraph models used as well as the epoch length for the Boston mTBI sample was longer than any of the other groups. To minimize the effects of these differences, all of the data were analyzed using the same software, visually inspected by similarly trained technicians, and verified against sleep diary data. It is possible that between-model differences account for some variability in the data. Additionally, the differing epoch length for the Boston mTBI sample may have reduced the sensitivity of the automatic scoring algorithm to sleep–wake transitions. We were unable to statistically control for these differences in the models (this variance is already captured by the group × location interaction term) and this remains a potential confound to these findings. Future multi-site studies employing consistent hardware and epoch lengths are needed in order address these concerns.

Finally, we were unable to capture any pre-injury data from the mTBI participants. Consequently, it is unclear what their level of premorbid sleep was. In spite of these important limitations, this study is the first reported multi-site actigraphy-based sleep study with an mTBI-only (rather than mixed severity) sample. These findings provide critical insight into the need for multi-site post-mTBI sleep related research that additionally addresses diverse clinical profiles of mTBI presentation, geographic and seasonal variation in sleep, and the relationship between objective measurement and subjective perceptions of sleep.

5. Conclusions

Sleep quality, particularly night-to-night sleep onset latency and sleep efficiency variability, are likely affected by mTBIs. While between-group differences in each site were apparent for these measures, the patterns of differences were not consistent across the two sites in this study. This highlights the fact that post-mTBI sleep outcomes reported from a single cohort may be insufficient to capture the spectrum of sleep disruption following injury. Furthermore, these findings suggest the possibility of multiple, rather than a singular, profile of sleep disruption following mTBI. Additionally, these results further confirm that self-reported and objectively quantified sleep quantity and quality following mTBI are largely unrelated. Precision medicine models derived from large cohorts across multiple sites are warranted to determine whether multiple sleep disruption profiles do indeed exist following mTBI and the conditions (eg, injury mechanism, other symptom presentation, social pressures) that may predispose or contribute to an individual's experience of sleep disruption.

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Conflicts of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2018.09.018.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2018.09.018.

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