



ORIGINAL ARTICLE

**Prior sleep problems and adverse post-traumatic  
neuropsychiatric sequelae of motor vehicle collision in the  
AURORA study**

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## Abstract

**Study Objectives:** Many patients in Emergency Departments (EDs) after motor vehicle collisions (MVCs) develop post-traumatic stress disorder (PTSD) or major depressive episode (MDE). This report from the AURORA study focuses on associations of pre-MVC sleep problems with these outcomes 8 weeks after MVC mediated through peritraumatic distress and dissociation and 2-week outcomes.

**Methods:** A total of 666 AURORA patients completed self-report assessments in the ED and at 2 and 8 weeks after MVC. Peritraumatic distress, peritraumatic dissociation, and pre-MVC sleep characteristics (insomnia, nightmares, daytime sleepiness, and sleep duration in the 30 days before the MVC, trait sleep stress reactivity) were assessed retrospectively in the ED. The survey assessed acute stress disorder (ASD) and MDE at 2 weeks and at 8 weeks assessed PTSD and MDE (past 30 days). Control variables included demographics, MVC characteristics, and retrospective reports about PTSD and MDE in the 30 days before the MVC.

**Results:** Prevalence estimates were 41.0% for 2-week ASD, 42.0% for 8-week PTSD, 30.5% for 2-week MDE, and 27.2% for 8-week MDE. Pre-MVC nightmares and sleep stress reactivity predicted 8-week PTSD (mediated through 2-week ASD) and MDE (mediated through the transition between 2-week and 8-week MDE). Pre-MVC insomnia predicted 8-week PTSD (mediated through 2-week ASD). Estimates of population attributable risk suggest that blocking effects of sleep disturbance might reduce prevalence of 8-week PTSD and MDE by as much as one-third.

**Conclusions:** Targeting disturbed sleep in the immediate aftermath of MVC might be one effective way of reducing MVC-related PTSD and MDE.

### Statement of Significance

Many people treated in EDs after motor vehicle collisions (MVCs) develop post-traumatic stress disorder (PTSD) or major depressive episode (MDE). Pre-MVC sleep disturbance, assessed with simple survey instruments in the ED, predicted 8-week development of both PTSD (through an association with 2-week ASD) and MDE (through associations with the transition between 2-week and 8-week MDE). Estimates suggest that eliminating these pre-MVC sleep problems or blocking the causal effects underlying their associations with the 8-week outcomes might reduce the prevalence of PTSD and MDE by as much as one-third. Targeting disturbed sleep in the immediate aftermath of an MVC might be effective in reducing MVC-related PTSD and MDE prevalence.

**Key words:** insomnia; major depressive episode; motor vehicle collision; nightmares; post-traumatic stress disorder; prospective design; sleep stress reactivity

## Introduction

Forty million Americans come to an emergency department (ED) after a traumatic experience each year [1]. Substantial proportions of these patients (10%–32%) are estimated to develop adverse chronic post-traumatic neuropsychiatric sequelae (APNS) [2–5], including post-traumatic stress disorder (PTSD), major depressive episode (MDE), post-concussion syndrome (PCS), and chronic pain [1, 6–8]. These APNS are an important source of population morbidity and mortality [9, 10] that are partially preventable because opportunities exist to develop preventive interventions in the immediate aftermath of trauma exposure. Efforts to develop these early interventions are hampered, though, by the fact that integrated research on the pathogenesis of APNS at the molecular, neural, physiological, cognitive, and behavioral levels is only in its infancy [11].

The scale and complexity of the work needed to address existing knowledge gaps in this area require a programmatic

approach. Recognizing this fact, the National Institute of Mental Health recently initiated a cooperative effort, the AURORA (Advancing Understanding of RecOverY afterR trauma) study, to collect a broad range of biobehavioral data from thousands of trauma survivors recruited from EDs and followed for 1 year [12]. In initial AURORA reports, we focused on AURORA respondents experiencing motor vehicle collision (MVC), the most common life-threatening traumatic experience in industrialized countries [13]. We examined patterns and associations of several predictors for acute stress disorder (ASD) and PTSD [14] and MDE [15] 2-weeks and 8-weeks post-MVC. These predictors included PTSD and MDE in the 30 days before the MVC along with sociodemographic characteristics and MVC experiences. And we examined mediation through peritraumatic distress and peritraumatic dissociation. Several significant gross associations were found of the baseline predictors with the 8-week outcomes, but virtually all these associations were entirely

mediated either by peritraumatic symptoms or by 2-week outcomes. These results suggest that the first 2 weeks after trauma may be a uniquely important time period for intervening to prevent and reduce the risk of PTSD and MDE 8 weeks after trauma exposure, but also raise important questions about the pre-trauma determinants of PTSD and MDE persistence between 2-weeks and 8-weeks post-trauma.

We begin the current report by presenting information about the associations of sleep problems in the 30 days before the MVC with 8-week PTSD and MDE as mediated through peritraumatic symptoms and 2-week outcomes. Extensive literature finds that preexisting sleep disturbances predict onset of both MDE [16–25] and PTSD [22, 23, 26, 27]. These observations about time-lagged associations argue against the idea that sleep complaints are nothing more than consequences or components of these neuropsychiatric disorders. Sleep has been hypothesized to have a causal role in the pathogenesis of trauma-related disorders via effects on learning and memory, executive function, and emotion regulation [28]. Sleep has also been linked with other causal pathways including inflammation, circadian rhythms, neurohormones, and monoaminergic neurotransmitters [29, 30]. Disturbed sleep may also be a proxy for other causal drivers of APNS [31]. Most longitudinal studies focused on pre-trauma insomnia, which has been typically assessed with retrospective self-report scales, as a predictor of incident MDE and PTSD over follow-up periods between 3 months to several years. A smaller number of studies probed other aspects of pre-trauma disturbed sleep or sleep duration as predictors of the same outcomes [23, 32, 33]. However, none of these studies attempted to trace out intervening pathways of these associations through peritraumatic symptoms or symptoms in the first few weeks after trauma exposure. This is our focus in the current report.

Our goal in focusing on these mediating pathways is to gain insights into the time windows over which sleep interventions might be expected to have effects on APNS. Specifically, we began by examining associations of five pre-MVC sleep characteristics with PTSD and MDE 8 weeks after MVC controlling for sociodemographics and MVC characteristics. We then estimated the extent to which these associations are mediated by peritraumatic distress and dissociation assessed in the ED in the immediate aftermath of the MVC and by subsequent symptoms assessed in a 2-week follow-up survey. Finally, we quantified the strength of gross associations between pre-MVC sleep and 8-week outcomes by estimating population attributable risk proportions (PARPs) to assess the potential impact of interventions aimed at addressing sleep problems in the wake of MVC. The PARP estimate represents the predicted proportion of observed cases of PTSD and MDE that we would expect to be prevented if the associations of the pre-MVC sleep variables were due to causal effects and these effects were removed [34].

## Methods

### Participants

AURORA enrollment began September 2017. Cases considered here are from the first data freeze and include only patients who completed 8-week assessments before April 2019. This cutoff was chosen to yield sufficient cases for preliminary descriptive

analyses early enough in the field process to allow mid-course corrections if data challenges were detected. Enrollment occurred at 23 urban EDs across the United States. Enrollment focused on individuals ages 18–75 presenting within 72 h of MVC who could speak and read English, were oriented to time-space and able to follow the enrollment protocol, were physically able to use a smart phone and possessed a smart phone for >1 year (Supplementary Figure S1). We excluded patients with a solid organ injury Grade >1 based on the American Association for the Surgery of Trauma criteria, significant hemorrhage, need for a chest tube or operation with general anesthesia, or likely to be admitted for >72 h. A total of 1,028 patients were either enrolled 67 days or more before March 25, 2019 or had completed the week 8 survey by that date, met all the above criteria, provided informed consent, and completed baseline assessments in the ED. In the current analysis, we focus on the 666 such participants who completed a 2-week survey (Mean [25th–75th percentiles]) 9.7 (7–11) days after MVC and an 8-week survey 50.5 (46–52) days after MVC.

### Measures

After providing written informed consent, each participating patient received an interviewer-administered ED assessment with both self-report questions and biological sample collections described elsewhere [12]. Subsequent 2- and 8-week web surveys were sent by text or email for self-completion or were completed with telephone interviewer assistance. Each patient was reimbursed \$60 for the ED assessment, \$40 for the 2-week survey, and \$40 for the 8-week survey. These procedures were approved by each participating institution's institutional review board through a central IRB. All questions were based on validated scales but in most cases, shortened to reduce patient burden.

#### Pre-MVC sleep

Patients answered a series of questions in the ED about sleep in the 30 days before the MVC to assess four constructs: (1) insomnia, (2) nightmares, (3) sleep duration, (4) daytime sleepiness, and (5) sleep stress reactivity.

Insomnia was assessed with the seven-question Insomnia Severity Index (ISI) [35]. The ISI asks about early (i.e. difficulty getting to sleep), middle (i.e. difficulty staying asleep), and late (i.e. waking too early in the morning) insomnia along with nonrestorative sleep (i.e. lack of satisfaction with sleep) and various aspects of distress-impairment due to sleep problems (interference with daytime activities, how noticeable the interference is, and how worrisome the interference is). Responses to the seven questions (Cronbach's  $\alpha = 0.87$ ) were summed (0–28 scale) and standardized to a mean of 0 and variance of 1.

Nightmares were assessed with modified questions from the Clinician-Administered PTSD Scale for DSM-IV [36] that asked how often the patient had unpleasant dreams using a 0–4 response scale (never, less than once a week, 1–2 nights a week, 3–4 nights a week, and every or nearly every night) and how much “distress or discomfort” these unpleasant dreams caused (none; mild, you might not have woken up; moderate, you easily went back to sleep; severe, you had difficulty going back to sleep; and extreme, you could not go back to sleep). The modification from the original was that the questions were asked about nightmares in general in the 30 days before the MVC rather than

in the original scale about nightmares regarding a specific prior trauma. Responses to the two questions ( $r = 0.67$ ) were summed and standardized to a mean of 0 and variance of 1.

Sleep duration was assessed using the question from the Pittsburgh Sleep Quality Index [37] about typical hours of sleep at night in the prior 30 days, with scores of 0 for >7 h, 1 for 6–7 h, 2 for 5–6 h, and 3 for <5 h.

Daytime sleepiness was assessed with two questions from the PROMIS Sleep-Related Impairment Short-Form 8a [38] on how often it was difficult to stay awake during the day (0–4 for never, less than once a week, 1–2 days a week, 3–4 days a week, and every or nearly every day) and how difficult it was to get things done because of this daytime sleepiness (0–4 for not at all, a little, somewhat, a lot, and extremely). Responses to the two questions ( $r = 0.48$ ) were summed and standardized to a mean of 0 and variance of 1.

In addition to these 30-day sleep assessments, sleep stress reactivity was assessed as a trait in the ED with two questions from the Ford Insomnia Response to Stress Test. The questions asked about difficulty sleeping at night (1) after a stressful experience during the day or (2) after getting bad news during the day [39]. Responses on a 0–4 scale (never, rarely, sometimes, often, and very often) ( $r = 0.71$ ) were summed and standardized to a mean of 0 and variance of 1.

#### Peritraumatic distress and dissociation

Peritraumatic distress and dissociation were assessed in the ED with a rationally selected 8-item short-form of the 13-item Peritraumatic Distress Inventory (PDI [40]) and the 5-item revised Michigan Critical Events Perception Scale (MCEPS [41]) (Supplementary Table S1). We modified the introduction to both series to ask about the frequency of feelings and experiences “during and immediately after” the MVC and used a 0–4 response scale of none of the time, a little, some, most, and all or almost all the time. Exploratory factor analysis with Promax rotation ( $r = 0.41$  between factors) confirmed a strong 2-factor structure (Cronbach’s  $\alpha = 0.80$  for PDI and 0.77 for MCEPS), with responses summed to create 0–32 PDI and 0–20 MCEPS scales and then standardized to a mean of 0 and variance of 1 for ease of interpretation.

#### ASD and PTSD

The PTSD Checklist for DSM-5 (PCL-5 [41]) was administered in the ED for PTSD in the 30 days before the MVC. The same scale was administered in the 8-week survey to assess PTSD in the past 30 days. The PCL-5 is a 20-item self-report scale that uses a 0–4 response format indicating how much the participant was “bothered by” each of the 20 DSM-5 Criteria B–E symptoms of PTSD (not at all, a little bit, moderately, quite a bit, and extremely) in the past 30 days. We used both the continuous 0–80 symptom score (Cronbach’s  $\alpha = 0.96$ ) standardized to a mean of 0 and variance of 1 and a dichotomous diagnostic classification for the 30 days before the MVC as predictors of 8-week PTSD diagnoses. Several different diagnostic classification rules have been proposed for the PCL-5 [42, 43]. We used the 31+ threshold based on findings from Bovin et al., who found that cut point (validated with the CAPS-5) was optimal for balancing false positives and false negatives [43]. We also assessed DSM-5 Acute Stress Disorder Criteria B in the 2-week survey (for symptoms in the past 2 weeks). DSM-5 stipulates 14 Criterion B symptoms,

9 or more of which are required for an ASD diagnosis. The 11 of these 14 that are also DSM-5 symptoms of PTSD (PTSD Criteria B1–4, C1–2, E1, and E3–6) were assessed with items from the PCL-5. The other three (anhedonia, dissociation, and amnesia) were assessed using items from the DSM-IV version of the PCL (amnesia), the PROMIS depression scale (anhedonia), and the Brief Dissociative Experiences Scale (DES-B)-Modified [44] (dissociation). In addition to defining this diagnosis, we summed continuous scores across the 14 symptoms to create an ASD symptom severity scale (Cronbach’s  $\alpha = 0.95$ ) standardized to a mean of 0 and variance of 1.

#### Major depression

Major depression was assessed with the PROMIS Depression Short-Form 8b [45], an 8-item scale used to measure recent symptoms of depression. The scale was administered in the ED for the 30 days before the MVC, in the 2-week survey for symptoms in the past 2 weeks, and in the 8-week survey for symptoms in the past 30 days. Respondents indicated how often they experienced each symptom using a 1–5 response scale (none of the time, a little, some, most, and all or almost all the time). Raw scores were summed (8–40 scale) and converted to a T-score (continuous scale) with a mean of 50 and a standard deviation of 10 relative to the general United States population. Cronbach’s  $\alpha$  was 0.95–0.97 across assessments. Consistent with PROMIS guidelines, a T-score of 60+ (i.e. 1 standard deviation above the mean in the general US population) was used as the threshold for defining a moderate to severe MDE [46]. The continuous baseline and 2-week scales were then transformed to a mean of 0 and variance of 1 to facilitate interpretation associations of these scales with the 8-week outcomes.

#### Control variables

As detailed in previous AURORA reports [14, 15], information was recorded in the ED about sociodemographics (age, sex, race-ethnicity, marital status, education, family income, and employment status), key characteristics of the MVC (e.g. patient was a driver versus passenger, severity of vehicular damage, and injuries sustained by people other than the participant), and information about the patient’s injuries. The latter included traumatic brain injury defined by diagnosed concussion or self-report of hitting head with loss of consciousness, amnesia, or disorientation [47]; severity of injury based on Abbreviated Injury Scale [48]; admission versus discharge from the ED; and patient self-ratings of current overall pain and other symptoms compared to the prior 30 days.

We also controlled for retrospective patient reports in the ED about pre-MVC (in the 30 days before the MVC) PTSD, MDE, pain, and other somatic symptoms. PTSD and MDE were assessed using the same continuous measures described above. Pain was assessed with the Pain Intensity Numeric Rating Scale (PI-NRS [49]), a single-item measure of “usual intensity” of physical pain on a 0–10 scale, where 0 was defined as no pain or tenderness and 10 as severe pain or tenderness, in each of 18 body regions [50]. The 18 scores were summed to create a body region pain severity scale (Cronbach’s  $\alpha = 0.82$ ) that was standardized to a mean of 0 and variance of 1. Similar questions were asked about severity of 20 somatic symptoms (Supplementary Table S2) with a 0–10 response scale asking “how much of a problem” each symptom was, where 0 was defined as no problem and 10 as

a major problem. These 20 symptoms included 8 adapted from the Pennebaker Inventory of Limbic Languidness scale [51], a 54-item scale used to assess frequency of physical symptoms/sensations and 12 adapted from the Rivermead Post-Concussion Symptoms Questionnaire [52], a scale of the severity of 16 PCS symptoms after head injuries. Exploratory factor analysis found that a single factor solution provided the best fit to the correlations among these 20 items, leading us to sum the 20 scores to create a single score of pre-MVC somatic symptoms (Cronbach's  $\alpha = 0.85$ ) that was standardized to a mean of 0 and variance of 1.

### Statistical analysis

Previous AURORA reports detail initial results regarding predictive bivariate and multivariate associations of (1) pre-MVC PTSD and MDE with peritraumatic symptoms, 2-week ASD and MDE, and 8-week PTSD and MDE and (2) associations of sociodemographic and MVC characteristics with peritraumatic symptoms, the 2-week outcomes, and the 8-week outcomes [14, 15]. We present here the results of an expanded series of models that add information about pre-MVC sleep as predictors of peritraumatic distress and dissociation, the 2-week outcomes, and the 8-week outcomes both with and without controls for the intermediate outcomes, in all cases controlling for pre-MVC outcome scores. The latter decompositions allow us to examine the extent to which the gross associations of pre-MVC sleep characteristics with the 8-week outcomes are mediated by peritraumatic symptoms and the 2-week outcomes. The models were simple logistic regression models without adjustments for loss to follow-up, as preliminary analysis found that the patients with complete 2-week and 8-week data did not differ significantly (1) from the original baseline sample in retrospectively reported pre-MVC APNS, peritraumatic distress, or peritraumatic dissociation or (2) from patients with 2-week data who did not provide 8-week data on 2-week symptoms (Supplementary Table S3). Patients with complete data did differ somewhat from those lost to follow-up on several sociodemographic variables, but these were controlled in all models. We did not use a multi-level modeling approach to adjust for clustering across the 23 EDs because of the small sample size and absence of evidence for clustering in preliminary analyses. However, we will use multilevel models in confirmatory analyses once the AURORA sample size increases.

We quantify the strength of gross associations between sleep and 8-week outcomes by calculating PARPs [53]. This is done by changing model coefficients to indicate that no associations exist between the sleep measures and the outcomes and then recomputing predicted probabilities of the outcomes based on those changes. Predicted prevalence estimates under the revised model are then calculated and compared with those observed. Estimated PARP is defined as the proportional reduction in estimated prevalence under the model, which can be interpreted under a causality assumption as the proportional reduction in the outcome if an intervention was able either to treat the sleep problems successfully or prevent these problems from affecting 8-week PTSD or MDE. All analyses were carried out using SAS Version 9.4 [54].

There was only a small amount of item-level missing data in the sample. These values were imputed using central tendency imputations. No attempt was made to weight the data to adjust for differences between participants and patients

who refused to participate given lack of information about non-participants. Logits and logits  $\pm 2$  standard errors were exponentiated to create odds ratios (ORs) with 95% confidence intervals (CIs). Statistical significance was evaluated using 0.05-level two-sided tests without corrections for multiple comparisons.

## Results

### Associations among the pre-MVC sleep variables

The four sleep measures out of the five that define sleep problems (insomnia, nightmares, daytime sleepiness, and sleep stress reactivity) had Pearson correlations with each other in the range 0.37–0.70 and factor loadings in the range 0.66–0.91 on a single factor in an exploratory factor analysis (Table 1). Based on the latter result, a composite sleep problems score was created by standardizing each score, summing, and then re-standardizing the composite to a mean of 0 and variance of 1. Sleep duration was inversely correlated with all four sleep problem measures (0.01–0.15) and forms a second factor in the exploratory factor analysis.

### Prevalence estimates of 2-week and 8-week outcomes

Prevalence estimates were 41.0% for 2-week ASD, 30.5% for 2-week MDE, 42.0% for 8-week PTSD, and 27.2% for 8-week MDE (Table 2). The ORs of the four diagnoses with each other were all very high (ORs = 8.0–24.6) (Table 2). One implication of this is that conditional probabilities of 8-week disorders were much higher among respondents who met criteria for the 2-week disorders (50.2%–76.4%) than among those who did not meet criteria for the 2-week disorders (11.2%–27.0%). Nonetheless, substantial proportions of respondents with 8-week PTSD (27.5%) and MDE (29.8%) did not meet criteria for these disorders in the 2-week surveys (Supplementary Table S4).

### Associations of pre-MVC sleep variables with peritraumatic distress and dissociation

Preliminary multivariate models were developed to predict peritraumatic distress and dissociation from data collected in the ED about sociodemographics, trauma characteristics, and retrospective reports about pre-MVC (i.e. in the 30 days before the MVC) PTSD, MDE, pain, and other somatic symptoms. Results of these models are reported elsewhere [14, 15]. We controlled for the significant variables in these models by examining incremental univariate associations of each pre-MVC sleep measure with each peritraumatic symptom score (Table 3). The sleep stress reactivity measure was the only significant sleep measure in these models, with standardized partial regression coefficients of  $\beta = 0.12$  predicting peritraumatic distress and  $\beta = 0.09$  predicting peritraumatic dissociation.

### Associations of pre-MVC sleep variables with 2-week ASD and 8-week PTSD

Three of the sleep measures (nightmares, insomnia, and sleep stress reactivity) and the sleep problems composite measure were significant predictors of 8-week PTSD (OR = 1.3–1.5) in

**Table 1.** Associations among the pre-MVC sleep variables in the Freeze 1 AURORA MVC sample (n = 666)\*

	Pearson correlations					Factor loadings		
	1	2	3	4	5	F1*	F1†	F2†
1. Insomnia	1.0	–	–	–	–	0.91	0.84	–0.19
2. Nightmares	0.47	1.0	–	–	–	0.65	0.79	0.25
3. Sleep duration	–0.15	0.01	1.0	–	–	–0.44	0.05	0.97
4. Daytime sleepiness	0.66	0.37	–0.08	1.0	–	0.76	0.80	0.04
5. Sleep stress reactivity	0.70	0.38	–0.14	0.42	1.0	0.80	0.71	–0.22

MVC, motor vehicle collision.

\*Unrotated factor loadings in a one-factor principal axis exploratory factor analysis.

†Promax rotated factor loadings in a two-factor principal axis exploratory factor analysis.

**Table 2.** Prevalence estimates and associations among 2-week and 8-week outcomes in the Freeze 1 AURORA MVC sample (n = 666)

	Prevalence		Associations					
	%	(SE)	2-week MDE		8-week PTSD		8-week MDE	
			OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
<b>Two-week outcomes</b>								
1. ASD	41.0	(1.9)	24.6	(15.5–39.1)	11.9	(8.2–17.2)	8.0	(5.4–11.8)
2. MDE	30.5	(1.8)			8.7	(5.9–12.8)	12.6	(8.5–18.9)
<b>Eight-week outcomes</b>								
1. PTSD	42.0	(1.9)					19.2	(12.0–31.0)
2. MDE	27.2	(1.7)						

MVC, motor vehicle collision; ASD, acute stress disorder; MDE, major depressive episode; PTSD, post-traumatic stress disorder; SE, standard error; OR, odds ratio; CI, confidence interval.

univariate models. The term “univariate models” refers to models that consider each sleep measure one at a time and control for sociodemographics, trauma characteristics, and retrospective ED reports about pre-MVC PTSD, MDE, pain, and other somatic symptoms (Table 4). The five sleep measures were also significant as a set in a multivariate version of this same model ( $\chi^2_5 = 12.9$ ,  $p = 0.025$ ). Decomposition shows that the same three sleep measures as in the univariate models for 8-week PTSD were significant univariate predictors of 2-week ASD both in a model that did not control for peritraumatic symptoms (OR = 1.3–1.5) and in a model that did control for peritraumatic symptoms (OR = 1.3–1.4). The same sleep measures were significant predictors of 8-week PTSD in a model that controlled for peritraumatic symptoms (OR = 1.3–1.5). However, all the sleep measures became non-significant in a model that additionally controlled for 2-week ASD in predicting 8-week PTSD (OR = 0.9–1.2).

### Associations of pre-MVC sleep variables with 2-week and 8-week MDE

Two of the sleep problems measures (nightmares and sleep stress reactivity) and the sleep problems composite measure were significant predictors of 8-week MDE (OR = 1.3–1.4) in univariate models (Table 5). The five sleep measures were also significant as a set in a multivariate version of this same model ( $\chi^2_5 = 13.4$ ,  $p = 0.020$ ). Decomposition shows that only the sleep problems composite measure was a significant predictor of 2-week MDE in the model that did not control for peritraumatic symptoms (OR = 1.3). None of the other two sleep measures was a significant univariate predictor of 2-week MDE either in a model that did not control for peritraumatic symptoms (OR = 1.2) or in a model that did control for peritraumatic symptoms (OR = 1.2). However, the sleep problems

composite measure and both of the other two sleep measures were significant predictors of 8-week MDE in a model that controlled for peritraumatic symptoms (OR=1.2–1.4) but only the sleep problems composite measure remained significant in a model for 8-week MDE that additionally controlled for 2-week MDE (OR = 1.4). Longer pre-MVC sleep duration was marginally protective for 8-week MDE in a model that controlled for peritraumatic symptoms and 2-week MDE, although it did not predict 2-week MDE. In other words, these pre-MVC sleep measures all predicted the transition in MDE between 2 and 8 weeks after MVC, but not earlier reactions to MVC. It is also noteworthy that when pre-MVC PTSD and MDE were removed as covariates, insomnia was a significant predictor of 8-week MDE both with (OR = 1.4) and without (OR = 1.7) controlling for 2-week MDE, similar to what has been reported in multiple prior studies [30].

### Population attributable risk proportions

PARP estimates suggest that sleep problems are associated with 31.9% of observed 8-week PTSD and 33.0% of 8-week MDE. If these associations are causal, the PARP estimates suggest that successful treatment of these sleep problems shortly after the MVC might lead to substantial reductions in 8-week PTSD and MDE.

### Discussion

The 8-week PTSD prevalence estimate of 42.0% in the Freeze 1 AURORA MVC sample, which we reported previously [14], is higher than estimates based on retrospective reports (0.2%–6.7%) in community surveys of people who had MVCs [55], but not substantially higher than in previous ED-based studies [5, 56, 57], suggesting that people who already have PTSD or who are at high

**Table 3.** Univariate associations of pre-MVC sleep measures with peritraumatic distress and dissociation controlling for significant baseline variables in the Freeze 1 AURORA MVC sample ( $n = 666$ )<sup>†</sup>

	Distress		Dissociation	
	<i>b</i>	(95% CI)	<i>b</i>	(95% CI)
Insomnia	-0.04	(-0.13 to 0.04)	0.02	(-0.07 to 0.11)
Nightmares	0.03	(-0.05 to 0.11)	0.02	(-0.06 to 0.10)
Sleep duration	-0.00	(-0.07 to 0.07)	-0.06	(-0.12 to 0.01)
Daytime sleepiness	0.02	(-0.06 to 0.09)	0.07	(-0.00 to 0.15)
Sleep stress reactivity	0.12*	(0.04 to 0.20)	0.09*	(0.01 to 0.17)
Composite sleep problems	0.05	(-0.04 to 0.15)	0.08	(-0.01 to 0.18)

MVC, motor vehicle collision; *b*, standardized partial regression of the peritraumatic symptom score on the pre-MVC sleep measure; CI, confidence interval.

\*Significant at the 0.05 level, two-sided test.

<sup>†</sup>Only one pre-MVC sleep measure was included in each model. All models controlled for significant associations of the outcomes with measures obtained in the ED of patient sociodemographics, trauma characteristics, and retrospective reports about pre-MVC (in the 30 days before the MVC) PTSD, MDE, pain, and other somatic symptoms.

**Table 4.** Univariate associations of pre-MVC sleep measures with 8-week PTSD as mediated through peritraumatic distress and dissociation and 2-week ASD, controlling for significant baseline predictors in the freeze 1 AURORA MVC sample ( $n = 666$ )<sup>†</sup>

	8-week PTSD		2-week ASD			8-week PTSD with controls				
	M1 <sup>‡</sup>		M2 <sup>‡</sup>		M3 <sup>‡</sup>		M4 <sup>‡</sup>		M5 <sup>‡</sup>	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Insomnia	1.3*	(1.0-1.6)	1.3*	(1.0-1.6)	1.3*	(1.0-1.6)	1.4*	(1.1-1.7)	1.2	(1.0-1.6)
Nightmares	1.3*	(1.1-1.6)	1.3*	(1.1-1.6)	1.3*	(1.0-1.5)	1.3*	(1.1-1.6)	1.2	(0.9-1.5)
Sleep duration	0.9	(0.8-1.1)	1.0	(0.9-1.2)	1.0	(0.8-1.2)	0.9	(0.8-1.1)	0.9	(0.7-1.1)
Daytime sleepiness	1.1	(0.9-1.4)	1.1	(0.9-1.4)	1.1	(0.9-1.4)	1.2	(1.0-1.4)	1.0	(0.8-1.3)
Sleep stress reactivity	1.3*	(1.1-1.6)	1.4*	(1.1-1.7)	1.3*	(1.0-1.6)	1.3*	(1.1-1.6)	1.1	(0.9-1.4)
Composite sleep problems	1.5*	(1.2-1.9)	1.5*	(1.2-1.9)	1.4*	(1.1-1.8)	1.5*	(1.2-1.9)	1.2	(0.9-1.6)

MVC, motor vehicle collision; PTSD, post-traumatic stress disorder; ASD, acute stress disorder; OR, odds ratio; CI, confidence interval.

\*Significant at the 0.05 level, two-sided test.

<sup>†</sup>Only one pre-MVC sleep measure was included in each model. All models controlled for significant associations of the outcomes with measures obtained in the ED of patient sociodemographics, trauma characteristics, and retrospective reports about pre-MVC (in the 30 days before the MVC) PTSD, major depressive episode (MDE), pain, and other somatic symptoms.

<sup>‡</sup>M1 = A series of five models to predict 8-week PTSD, each model including as predictors the controls mentioned in † and exactly one of the five pre-MVC sleep measures; M2 = A series of five models to predict 2-week ASD, each model including as predictors the controls mentioned in † and exactly one of the five pre-MVC sleep measures; M3 = The same as M2 other than adding the peritraumatic distress and peritraumatic dissociation measures as controls; M4 = The same as M1 other than adding the peritraumatic distress and peritraumatic dissociation measures as controls; M5 = The same as M4 other than adding the continuous 2-week ASD symptom score as a control. It is noteworthy that previous analyses reported elsewhere [14] found that no significant prediction accuracy is added by including splines for the peritraumatic symptoms scores or 2-week ASD symptom score or a dichotomous diagnostic classification for 2-week ASD to these models.

risk of PTSD might be more likely than others who experience an MVC to come to the ED when they are not seriously enough injured to be hospitalized. The clearest evidence for this is found in [Supplementary Table S3](#), which shows that PTSD prevalence in the 30 days prior to the MVC was already 28.2%, which compares to less than 5% in the total US population [58]. This might be due to an association of prior PTSD with MVC exposure, but a more likely explanation is an association of prior PTSD with coming to the ED despite not being seriously injured.

The 27.2% 8-week MDE prevalence estimate, also reported previously [15], is substantially higher than estimates in previous studies examining post-MVC psychopathology (7.8%) [59], but comparable to the estimate in a recent Australian study that recruited respondents using insurance information [60], possibly reflecting not only the same kind of selection process suggested above for PTSD but also that the threshold used to define MDE in AURORA was based on the recommended threshold for the PROMIS screening scale, which might not be consistent with the thresholds used in previous studies.

We are aware of only one other study that examined the associations of retrospectively reported pre-trauma sleep problems

with reactions to a traumatic event in a sample relatively comparable to the AURORA sample [22]. That study examined 1,033 traumatically injured patients admitted to hospitals and found that a measure of retrospectively reported general sleep disturbance in the 2 weeks before injury predicted PTSD, MDE, and other disorders 3 months after trauma exposure. Our results provide more textured information about the aspects of pre-trauma sleep disturbance (i.e. nightmares, insomnia, sleep duration, and sleep stress reactivity) that predict post-traumatic psychopathology. We also show that the associations of these measures with 8-week PTSD are due to prior associations with 2-week ASD and not with the transition from ASD to PTSD, whereas the opposite is true for the associations of these sleep measures with 8-week MDE, which are due to associations with the transition between 2-week and 8-week MDE rather than with earlier MDE. It is unclear why these differences exist in the timing of the effects on MVC-related PTSD and MDE, but we hope our planned future analyses of underlying biological processes as AURORA progresses will shed light on this question. In particular, we will be able to discern if objective measures of sleep duration, collected prospectively starting from the ED visit, exert effects on

**Table 5.** Univariate associations of pre-MVC sleep measures with 8-week MDE as mediated through peritraumatic distress and dissociation and 2-week MDE, controlling for significant baseline predictors in the freeze 1 AURORA MVC sample (n = 666)<sup>†</sup>

	8-week MDE		2-week MDE				8-week MDE with controls			
	M1 <sup>‡</sup>		M2 <sup>‡</sup>		M3 <sup>‡</sup>		M4 <sup>‡</sup>		M5 <sup>‡</sup>	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Insomnia	1.2	(0.9–1.5)	1.0	(0.8–1.3)	1.0	(0.8–1.3)	1.2	(0.9–1.4)	1.2	(0.9–1.6)
Nightmares	1.3*	(1.0–1.6)	1.2	(1.0–1.5)	1.2	(1.0–1.5)	1.2*	(1.0–1.5)	1.2	(1.0–1.6)
Sleep duration	0.8*	(0.6–1.0)	1.1	(0.9–1.3)	1.1	(0.9–1.3)	0.8*	(0.7–1.0)	0.7*	(0.6–0.9)
Daytime sleepiness	1.2	(1.0–1.5)	1.2	(1.0–1.5)	1.2	(1.0–1.5)	1.2	(0.9–1.4)	1.1	(0.9–1.5)
Sleep stress reactivity	1.3*	(1.0–1.7)	1.2	(1.0–1.6)	1.2	(0.9–1.5)	1.3*	(1.0–1.6)	1.2	(0.9–1.6)
Composite sleep problems	1.4*	(1.1–1.9)	1.3*	(1.0–1.7)	1.3	(1.09–1.7)	1.4*	(1.1–1.8)	1.4*	(1.0–1.8)

MVC, motor vehicle collision; MDE, major depressive episode; OR, odds ratio; CI, confidence interval.

\*Significant at the 0.05 level, two-sided test.

<sup>†</sup>Only one pre-MVC sleep measure was included in each model. All models controlled for significant associations of the outcomes with measures obtained in the ED of patient socio demographics, trauma characteristics, and retrospective reports about pre-MVC (in the 30 days before the MVC) PTSD, MDE, pain, and other somatic symptoms.

<sup>‡</sup>M1 = A series of 5 models to predict 8-week MDE, each model including as predictors the controls mentioned in <sup>†</sup> and exactly one of the 5 pre-MVC sleep measures; M2 = A series of 5 models to predict 2-week MDE, each model including as predictors the controls mentioned in <sup>†</sup> and exactly one of the 5 pre-MVC sleep measures; M3 = The same as M2 other than adding the peritraumatic distress and peritraumatic dissociation measures as controls; M4 = The same as M1 other than adding the peritraumatic distress and peritraumatic dissociation measures as controls; M5 = The same as M4 other than adding the continuous 2-week MDE symptom score as a control. It is noteworthy that previous analyses reported elsewhere [15] found that no significant prediction accuracy is added by including splines for the peritraumatic symptoms scores or 2-week MDE symptom scores or a dichotomous diagnostic classification for 2-week MDE to these models.

different features of APNS at different time points. The PARP estimates tell us this could be an important line of investigation, as the causal factors underlying the associations of the pre-MVC sleep problems with the 8-week psychopathological reactions to MVC examined are powerful, accounting for as much as one-third of all cases of 8-week PTSD and MDE. It is unclear from our data whether these causal effects are due to sleep problems or to some unmeasured causal risk factors that influence both pre-MVC sleep problems and the 8-week outcomes, but this uncertainty could be resolved with a pragmatic trial that intervened to help patients with preexisting sleep problems manage their sleep in the aftermath of their MVC.

It would be useful to elucidate causal pathways before attempting to implement such a trial. Sleep stress reactivity, which was found to be the most consistent predictor among those considered here, might be thought of as a poor target for intervention based on evidence that it is a trait-like characteristic that is stable over time and across various stressors [61, 62], and might not be easily modified because it is determined by genetics [63, 64]. However, evidence exists that sleep stress reactivity is malleable given that new-onset insomnia disorder is associated with increased sleep stress reactivity [65] and that sleep stress reactivity is influenced by cognitive factors, such as pre-sleep rumination [66], which can be effectively targeted for treatment [67]. We are not aware of any research that has tried to correct disturbed sleep by targeting cognitive determinants of sleep stress reactivity, but this might be a fruitful line of investigative intervention in the early aftermath of MVC among patients reporting preexisting sleep problems.

Pre-MVC nightmares were also found to be important in predicting both PTSD and MDE. This finding is consistent with prior studies that retrospectively reported bad dreams before Hurricane Andrew predicted general psychiatric morbidity 6–12 months following the hurricane [32] and that pre-deployment nightmares among members of the Dutch military predicted PTSD symptoms 6 months post-deployment to Afghanistan [33]. A plausible biological pathway is through rapid eye movement (REM) sleep given the suggestion that nightmares

are possibly an indicator of disturbed REM sleep [68] and evidence that REM fragmentation measured with polysomnography among traumatized patients predicts developing PTSD [69–71]. This association might be due to REM fragmentation impairing generalization of extinction learning hypothesized to play a role in the development and maintenance of PTSD [72]. Disturbed REM sleep has also long been associated with MDE [73]. This leads to the speculation that pharmacologic or behavioral sleep interventions that consolidate REM sleep might reduce the risk of post-traumatic psychopathology among patients reporting pre-trauma nightmares.

Pre-MVC insomnia was found to be important in predicting PTSD but not MDE. The failure to find an association with MDE is contrary to an extensive literature reviewed elsewhere [30]. However, unlike these previous studies, we included controls for both pre-trauma PTSD and pre-trauma MDE. When these covariates were removed, our results were the same as prior published studies in finding that pre-MVC insomnia predicts 8-week MDE. This suggests that the gross association of pre-MVC insomnia with 8-week MDE is due to confounding with preexisting APNS.

Six limitations of this initial AURORA report on sleep problems need to be noted. First, response bias might have been introduced by the low response rate. We are designing a brief non-respondent survey to evaluate this bias. Second, the number of participants is well below the number needed to estimate mediating pathways directly, leading us to focus on comparisons of univariate and multivariate associations rather than doing a formal decomposition. The latter will be carried out once the AURORA sample size increases. Third, the decision to carry out short-term follow-ups at 2 and 8 weeks was relatively arbitrary and resulted in not being able to detect DSM PTSD as of 1 month that remitted before 8 weeks. Some other prospective studies can do this because they included a 1-month assessment [74]. However, we are administering short smart phone symptom surveys to all respondents each day for the first 8 weeks after trauma exposure, allowing us to capture symptoms of PTSD and MDE in a more granular fashion. We will build in information



about these symptom assessments once the in-progress models for the temporal unfolding of these systems are finalized. Fourth, the pre-MVC sleep variables were assessed retrospectively in the ED after the MVC and might be colored by recall bias. We will soon be able to address this limitation indirectly by examining objective measures of sleep beginning the night after the initial ED visit obtained from a wearable device worn during sleep by all AURORA participants, allowing us to investigate the extent to which the associations of retrospectively-reported pre-MVC sleep with 8-week APNS are mediated by objective measures of sleep in the days and weeks after the MVC. Fifth, the many different constructs assessed in the baseline AURORA assessment were all based on abbreviated versions of original scales in order to minimize patient burden. Sixth, we focused only on 8-week outcomes. Meta-analysis shows that up to 25% of PTSD cases among people followed for several years after trauma exposure do not meet full PTSD criteria until more than 6 months later [75] and that a complex-fluctuating course of illness exists for many cases over as long as 24 months [76]. We were unable to study these complexities in this initial analysis because respondents were followed only for 8 weeks. However, all AURORA respondents are also being assessed at 3, 6, 9, and 12 months after MVC exposure, allowing us to examine delayed onset as well as other patterns of symptom changes over these time periods once these follow-up surveys have been completed.

This initial report on pre-MVC sleep problems in AURORA sought to investigate overall associations with 8-week PTSD and MDE as mediated through peritraumatic distress and dissociation and 2-week disorders. We found relatively high 8-week PTSD and MDE prevalence, substantial associations of pre-MVC sleep problems with these outcomes, no evidence that these associations were mediated through peritraumatic symptoms, evidence that the associations of these sleep problems with 8-week PTSD were mediated through 2-week ASD, and evidence that associations of sleep problems with 8-week MDE were mediated by the transition between 2-week and 8-week MDE. These results suggest that windows of opportunity for preventive intervention exist after MVC (the first 2 weeks for PTSD; 2–8 weeks for MDE), but the biological underpinnings of these associations remain to be elucidated and intervention implications explored.

## Supplementary material

Supplementary material is available at SLEEP online.

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