SLEEP DISTURBANCE, TRAUMA AND PSYCHIATRY DISORDERS

Sleep Disturbance Immediately Prior to Trauma Predicts Subsequent Psychiatric Disorder

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Study Objectives: This study investigated the extent to which sleep disturbance in the period immediately prior to a traumatic event predicted development of subsequent psychiatric disorder.

Design: Prospective design cohort study

Setting: Four major trauma hospitals across Australia

Patients: A total of 1033 traumatically injured patients were initially assessed during hospital admission and followed up at 3 months (898) after injury

Measures: Lifetime psychiatric disorder was assessed in hospital with the Mini-International Neuropsychiatric Interview. Sleep disturbance in the 2 weeks prior to injury was also assessed using the Sleep Impairment Index. The prevalence of psychiatric disorder was assessed 3 months after traumatic injury.

Results: There were 255 (28%) patients with a psychiatric disorder at 3 months. Patients who displayed sleep disturbance prior to the injury were more likely to develop a psychiatric disorder at 3 months (odds ratio: 2.44, 95% CI: 1.62–3.69). In terms of patients who had never experienced a prior disorder (n = 324), 96 patients (30%) had a psychiatric disorder at 3 months, and these patients were more likely to develop disorder if they displayed prior sleep disturbance (odds ratio: 3.16, 95% CI: 1.59–4.75).

Conclusions: These findings provide evidence that sleep disturbance prior to a traumatic event is a risk factor for development of posttraumatic psychiatric disorder.

Keywords: Sleep disturbance, insomnia, psychiatric disorder, trauma

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THERE IS CONVERGENT EVIDENCE THAT LIFETIME HISTORY OF INSOMNIA IS A RISK FACTOR FOR SUBSEQUENT PSYCHIATRIC DISORDER. STUDIES OF adults have repeatedly found that sleep disturbance is associated with greater risk for development of depression¹⁻⁵ and anxiety^{1,3} in adults. There is also evidence that sleep problems in children or adolescents is predictive of subsequent mental health problems.⁶

One possible reason for the relationship between sleep disturbance and subsequent psychiatric disorder is that impaired sleep may limit one's capacity to manage stressors that precipitate psychiatric disorder. Impaired sleep disturbance prior to a stressor may contribute to subsequent disorder because it (a) limits the cognitive resources available to manage the stress, (b) contributes to hyperarousal that may lead to psychiatric disorder, (c) represents an additional stressor that compounds the effect of the environmental stressor, or (d) limits restorative sleep that is required to manage stressful events. To date, no studies have directly examined the influence of sleep disturbance immediately prior to experiencing a marked stressor on development of subsequent psychiatric disorder. Previous epidemiological studies have typically studied the onset of chronic sleep disturbance prior to the onset of psychiatric disorder;

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however, this approach does not allow specification of the sleep disturbance immediately prior to a stressor that may precipitate psychiatric disorder. One small study reported that sleep disturbance prior to Hurricane Andrew was associated with increased risk of disorder following the trauma. This study's conclusions were limited, however, by obtaining reports of pre-trauma sleep functioning 6 months after the hurricane.

The current study aims to test the proposal that sleep disturbance immediately prior to traumatic stressor increases the risk of subsequent psychiatric disorder. This large longitudinal study of survivors of traumatic injury was conducted across 4 hospital sites and assessed sleep disturbance in the 2 weeks prior to the traumatic injury. Participants were re-assessed 3 months later to determine the relationship between sleep disturbance and development of a range of psychiatric disorders. We predicted that patients with sleep disturbance immediately prior to the traumatic injury would be more likely to develop posttraumatic psychiatric disorders. On the basis of convergent evidence that sleep disturbance is prevalent in many psychiatric disorders,8 it is important to ensure that the effect of sleep disturbance is not a proxy for the influence of prior psychiatric disturbance immediately prior to the trauma. Accordingly, this study assessed for lifetime psychiatric disorders, and controlled for prior disorder.

METHOD

Participants

Randomized admissions to 4 level 1 trauma centers across 3 states in Australia were recruited into the study between April 2004 and February 2006. The study was approved by

the research and ethics committee at each hospital. Inclusion criteria included no brain injury or mild traumatic brain injury (MTBI; defined as a loss of consciousness of \leq 30 min, Glasgow Coma Scale score 13-15 after 30 min, or posttraumatic amnesia $\leq 24 \text{ h}^9$); age between 16 and 70 years of age; ability to understand and speak English proficiently; and hospital admission > 24 h following traumatic injury. Individuals were excluded from the study if they had moderate or severe head injury; were currently psychotic or suicidal; were non-Australian visitors, cognitively impaired, or under police guard. Moderate or severe brain injury was excluded because these patients cannot reliably report onprior or current experiences because of ongoing post traumatic amnesia. Individuals who met entry criteria were randomly selected using an automated, random assignment procedure, stratified by length of stay. This approach was adopted to ensure that we did not differentially recruit patients who had longer hospital stays because they may be more accessible.

Procedure

Following written informed consent, trained clinicians conducted clinical interviews. Patients were assessed for current psychiatric disorders at the time of injury using the Mini-International Neuropsychiatric Interview (version 5.5; MINI).¹⁰ The MINI is a short, structured diagnostic interview based on the DSM-IV and the ICD-10 classification of mental illness. The MINI consists of a set of screening questions and a module for each diagnosis; modules are administered if a patient responds positively to a particular screening question. The MINI was used to assess lifetime psychiatric diagnoses including major depressive episode, panic disorder, agoraphobia, social phobia, obsessive compulsive disorder, posttraumatic stress disorder, generalized anxiety disorder, alcohol use disorder, and marijuana use disorder. The MINI has good reliability for all diagnoses when compared to the Composite International Diagnostic Interview (> 0.5 for all diagnoses except social phobia and generalized anxiety disorder). Information regarding demographic, hospital admission, and injury-related factors were obtained from medical records. Injury information included the Injury Severity Score, 11 (which is a measure of overall injury severity calculated on location and severity of injury assessed during the initial 24 h of hospital admission), and cause of traumatic injury, hospitalization length, and presence of MTBI. Sleep disturbance immediately prior to injury was assessed using a subset of the Sleep Impairment Index (SII). 12 The SII is a 7-item measure of sleep impairment; this study used 5 of the 7 items because of time constraints within a larger clinical interview. The items indexed impairment in sleep onset, maintenance, early waking, disturbance caused by sleep problems, and distress caused by sleep problems (this version omitted items indexing satisfaction with sleep and the extent to which sleep problems were noticeable by others). The internal consistency of the 5-item version was 0.87, and the item-total correlations varied from 0.46 (waking early) to 1.00 (delayed onset sleep), with a mean correlation of 0.57. These values are similar to the values reported for the 7-item measures, 13 and validate our use of the 5-item scale. Each item was rated on 5-point rating scale (0-4) providing a potential total score of 28, and the recommended cut-off for identifying insomnia was 14.14 Accordingly, because

we used 5 of the 7 items, we adopted a pro-rated score of 12 as a conservative index of sleep disturbance.

At 3 months after injury, participants were contacted by telephone and completed the MINI to assess current prevalence of psychiatric disorders. In addition, patients were assessed for posttraumatic stress disorder (PTSD) by using the Clinician Administered PTSD Scale-IV (CAPS-IV).15 The CAPS possesses good sensitivity (0.84) and specificity (0.95) relative to the Structured Clinical Interview for DSM Disorders PTSD diagnosis; it also possesses sound test-retest reliability (0.90). The CAPS was employed in addition to the MINI to identify the frequency and severity of PTSD after injury. Study interviewers were trained in the study protocol by a clinical psychologist (MOD), and all assessments were recorded to ensure ongoing adherence to the protocol. To assess interrater reliability, 5% of all CAPS and MINI interviews were rescored by examiners who were blind to the original scoring. Overall, the PTSD diagnostic consistency was strong for the CAPS ($\kappa = 1.00$) and the MINI (mean $\kappa = 0.99$) at 3 months.

DATA ANALYSIS

Demographic, injury characteristics, and sleep characteristic measures for participants and those lost to 3-month follow-up were compared using t tests for continuous measures or χ^2 for categorical measures with a Bonferroni adjustment ($\alpha = 0.005$) to allow for the multiple comparisons.

Subsequent analyses were reported by (a) excluding patients with prior psychiatric disorder and (b) including all patients but controlling for prior psychiatric disorder. We calculated odds ratios for patients who had sleep disturbance immediately prior to the injury and subsequent psychiatric disorder. The extent to which elevated sleep disturbance predicts subsequent disorder in relation to other factors that may account for posttraumatic adjustment was examined through hierarchical logistic regression. The order of factors entered in regression analyses was based on demographic and injury-related factors that might have influenced the effect of sleep disturbance on subsequent PTSD. In terms of patients with no prior disorder, at the first step we entered gender; at the second step we entered trauma mechanism; at the third step we entered patient's Injury Severity Score; at the fourth step we entered patient age; and at the fifth step we entered presence of sleep impairment prior to the injury. We repeated these factors in a logistic regression analysis to predict major depressive disorder (MDD), anxiety disorders, and substance use disorder at follow-up. Regressions that included all patients also added prior psychiatric disorder in the step before prior sleep disturbance.

RESULTS

Patient Characteristics

Of 1593 patients eligible for participation, 1166 (73%) agreed to participate, 1126 completed the MINI (71%) and 1033 (65%) completed the SII during admission. Table 1 presents a summary of patient characteristics. Four hundred thirty experienced an MTBI, and the mean injury severity score was 10.90 (SD = 8.06); the majority of patients suffered moderate or severe injuries (see Table 1). Participants spent an average of 12.47 (SD = 13.00) days in hospital. Individuals who refused to participate

in the current study did not differ from participants in terms of gender, days in hospital, injury severity score, or SII score.

At the 3-month follow-up assessment, 135 patients could not be contacted or declined to participate; 898 were interviewed by telephone, representing 87% of the initial sample who completed all baseline measures. Patients at the follow-up assessment did not differ from those who did not participate in terms of age, length of hospital stay, injury severity score, or initial SII score.

There were 599 (58% of those with complete baseline data) patients assessed at baseline with a lifetime history of psychiatric disorder, including major depression (26%), PTSD (14%), panic disorder (7%), agoraphobia (13%), social phobia (9%), obsessive compulsive disorder (8%), generalized anxiety disorder (10%), and substance use disorder (39%). Three hundred and twenty four patients with no prior disorder were assessed at 3 months.

Prevalence of Psychiatric Disorders at 3-Month Assessment

Table 2 presents the prevalence of each psychiatric disorder at 3 months, the proportion of participants with and without disorder who displayed sleep disturbance in the 2 weeks prior to the traumatic injury, and the odds ratio of developing a psychiatric disorder if prior sleep disturbance was present. These results indicated that psychiatric disorders were common even in patients with no prior disorder, with 96 patients (30%) of those followed up at three months who had no prior disorder (n = 324) developing a new psychiatric disorder. The most common disorders were major depression (15%), agoraphobia (13%), PTSD (11%), and generalized anxiety disorder (9%). In terms of receiving mental health assistance at 3 months, 147 (16%) patients indicated that they had consulted a mental health professional and 84 (9%) indicated that they were prescribed medication for "stress, depression, or sleep problems."

Table 2 indicates that sleep disturbance immediately prior to the traumatic injury posed significant risk for developing any of the psychiatric disorders 3 months later. When we included all patients (controlling for prior disorder), sleep impairment was a significant predictor; patients with sleep disorders prior to trauma were 2.44 times as likely to develop a psychiatric disorder as those who did not have sleep disorders prior to trauma. The hierarchical logistic regression indicated that developing any psychiatric disorder was predicted by female gender (Wald statistic: 5.61, P = 0.05) and sleep impairment (Wald statistic: 17.93, P = 0.001); developing PTSD was predicted by female gender (Wald statistic: 11.01, P = 0.001) and sleep impairment (Wald statistic: 10.79, P = 0.001); any anxiety disorder was predicted by female gender (Wald statistic: 5.70, P = 0.05) and sleep impairment (Wald statistic: 13.09, P = 0.001); panic disorder was predicted by female gender (Wald statistic: 6.12, P = 0.001) and sleep impairment (Wald statistic: 15.84); agoraphobia by sleep impairment (Wald statistic: 21.17, P = 0.001); social phobia by sleep impairment (Wald statistic: 3.99, P = 0.05), obsessive compulsive disorder by sleep impairment (Wald statistic: 11.92, P = 0.001); generalized anxiety disorder by sleep impairment (Wald statistic: 4.93, P = 0.03); any anxiety disorder by sleep impairment (Wald statistic: 6.13, P = 0.001); substance use disorder by younger age female gender (Wald statistic: 12.36, P = 0.001) and sleep impairment (Wald statistic:

3.73, P = 0.05); and major depression was predicted by female gender (Wald statistic: 3.88, P = 0.05) and sleep impairment (Wald statistic: 19.67, P = 0.001).

In terms of patients who had no prior psychiatric disorder, patients were 3.16 times as likely to develop a psychiatric disorder if they had sleep disturbance prior to the trauma as those who did not have sleep disturbance. Social phobia was the one diagnosis that was not associated with prior sleep disturbance. The hierarchical logistic regression indicated that developing any psychiatric disorder was predicted by female gender (Wald statistic: 5.42, P = 0.05) and sleep impairment (Wald statistic: 18.75, P = 0.001); developing PTSD was predicted by female gender (Wald statistic: 14.55, P = 0.001) and sleep impairment (Wald statistic: 10.63, P = 0.001); any anxiety disorder was predicted by female gender (Wald statistic: 5.70, P = 0.05) and sleep impairment (Wald statistic: 13.09, P = 0.001); major depression was predicted by female gender (Wald statistic: 6.00, P = 0.051) and sleep impairment (Wald statistic: 18.57, P = 0.001); and substance use disorder was predicted by younger age (Wald statistic: 5.62, P = 0.05) and sleep impairment (Wald statistic: 10.18, P = 0.001) (Table 2).

DISCUSSION

This study provides the first large-scale multi-site evidence that sleep disturbance immediately prior to exposure to a traumatic event poses a significant risk for development of a range of psychiatric disorders, including PTSD, other anxiety disorders, major depression, and substance use disorders. By controlling for the effect of prior psychiatric disorder, we demonstrated that this influence is independent of the contribution of psychiatric disorders that may be associated with prior sleep disturbance. Most impressively, sleep disturbance predicted subsequent psychiatric disorder development beyond the effects of age, gender, mechanism of traumatic injury, severity of injury, and prior psychiatric disorder. The current findings accord with much evidence that chronic insomnia is a solid predictor in adults of subsequent psychiatric disorder.1-4 The pattern of sleep disturbance preceding the onset of psychiatric disorders has been established in large-scale studies,3 as well as one small study that pointed to pre-trauma sleep disturbance being associated with subsequent psychiatric disorder. 16 The current finding advances previous findings by clarifying that sleep disturbance immediately prior to a major stressor does contribute to subsequent disorder.

There are several possible explanations for the observed findings. We premise these explanations by acknowledging that there may be common mechanisms for the relationship across disorders or there may be disorder-specific mechanisms underpinning the risk posed by sleep disturbance immediately prior to trauma. One possible explanation is that impaired sleep prior to the traumatic injury may deplete the emotional, cognitive, and physical resources required to optimally manage the aftermath of a traumatic experience. Fatigue is a common problem associated with sleep disturbance.¹⁷ Cognitive impairments, including poor concentration and attention, are also commonly reported in insomniacs.¹⁸ People who are depleted in these domains may have difficulty in managing the stress of a traumatic injury. There is evidence that pre-trauma intelligence¹⁹ and capacity to appraise events in a realistic way²⁰ prior to trauma are

Table 1—Demographic characteristics of the sample (N = 1033)

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Gender	N	%	
Male	752	73.0	
Female	281	27.0	
Age (y)			
18-24	203	19.7	
25-34	230	22.3	
35-44	230	22.3	
45-54	200	19.4	
55-64	114	11.0	
> 65	25	2.4	
Ethnic Status			
Caucasian	909	88.0	
Other	124	12.0	
Marital Status			
Married/de facto	504	48.8	
Single	529	51.2	
Employment Status			
Employed	823	79.7	
Unemployed	53	5.1	
Not in labour force	157	15.2	
Education			
Bachelor degree or above	173	16.7	
Diploma	59	5.7	
Vocational qualification	378	36.6	
High school only	423	41.0	
Type of Traumatic Injury			
Motor vehicle accident	666	64.5	
Industrial accident	71	6.9	
Assault	62	6.0	
Traumatic fall	157	15.2	
Other	77	7.4	
Injury Severity Score			
Minimum	77	7.5	
Moderate	298	28.8	
Severe	457	44.2	
Serious	138	13.4	
Critical	63	6.1	

Table 2—Prevalence of sleep disturbance at time of injury for each psychiatric disorder at 3 months

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Including Prior Psychiatric Disorder		hiatric order	% with Sleep Disturbance		Association with sleep disturbance	
(n = 898)	N	%	Diagnosis	No Diagnosis	OR	95% CI
PTSD	67	7.5	28.4	14.1	2.56**	1.46-4.94
Panic disorder	46	5.1	34.8	14.0	4.07**	2.04-8.12
Agoraphobia	95	10.5	32.6	13.0	3.40**	2.02-5.73
Social phobia	43	4.8	32.6	14.2	2.19*	1.01-4.76
OCD	21	2.3	42.9	14.4	5.05**	2.01-12.68
GAD	78	8.7	26.9	14.0	1.97*	1.08-3.58
Any anxiety disorder	181	20.2	26.5	12.3	2.47**	1.59–3.84
Major depression	147	16.3	28.6	12.5	2.81**	1.78–4.44
Substance use disorder	56	6.2	25.0	14.4	2.05*	1.01-4.24
Any psychiatric disorder	255	28.4	24.7	11.4	2.44**	1.62–3.69
Excluding Prior Psychiatric Disorder (n = 324)						
PTSD	34	10.5	18.8	9.1	2.89**	2.06-9.79
Panic disorder	16	4.9	8.3	4.3	2.17	0.65-7.24
Agoraphobia	41	12.7	27.1	10.1	3.48**	1.57-7.71
Social phobia	10	3.1	0.0	3.6	0.01	0.01-0.02
OCD	10	3.1	12.5	1.4	11.44**	2.90-45.16
GAD	29	9.0	12.5	8.3	1.07	0.34-3.36
Any anxiety disorder	72	22.2	37.5	19.6	2.50*	1.23-5.09
Major depression	50	15.4	35.4	12.0	3.98**	1.87–6.25
Substance use disorder	19	5.9	14.6	4.3	3.90**	1.31–11.59
Any psychiatric disorder	96	29.6	52.1	29.7	3.16**	1.59-4.75

^{**}P < 0.001, * P < 0.05. For cases excluding prior psychiatric disorder, odds ratios calculated after controlling for gender, mechanism of injury, age, and injury severity score. For cases including prior psychiatric disorder, odds ratios calculated after controlling for gender, mechanism of injury, age, injury severity score, and prior psychiatric disorder.

protective against PTSD development after trauma exposure. The cognitive impairments associated with sleep disturbance may limit these functions and contribute to subsequent psychiatric disorder.

Many models of insomnia are based on hyperarousal being fundamental to the disorder.²¹ These models posit that hyperarousal underpins chronic insomnia and that this can involve cardiovascular or neuroendocrine levels of arousal. It is possible that sleep disturbance immediately prior to trauma renders the individual more susceptible to developing a psychiatric disorder, especially an anxiety disorder, because their propensity for fear conditioning prior to trauma may be augmented by increased arousal levels. Prevailing models of PTSD propose that extreme sympathetic arousal at the time of a traumatic event can result in the release of stress neurochemicals (including norepinephrine and epinephrine) that mediate an overconsolidation of

trauma memories.²² There is evidence that hyperreactivity prior to trauma exposure predicts subsequent posttraumatic stress.²³ It is possible that elevated arousal associated with sleep disturbance contributes to greater anxiety reactions to trauma, and this leads to greater rates of subsequent psychiatric disorder.

Sleep disturbance itself may represent a stressor that compounds posttraumatic adjustment difficulties. There is considerable evidence that PTSD is influenced by the degree of stressors experienced in the posttraumatic period. ^{24,25} Considering the documented impairments experienced by people with insomnia, ¹⁸ it is possible that trauma survivors who also experience preexisting sleep disturbance may be more likely to develop a psychiatric disorder because they have the compounded stressors of the traumatic event, the stressful experiences that may occur in the posttraumatic period, and the problems caused by sleep disturbance.

PTSD = posttraumatic stress disorder.

OCD = obsessive compulsive disorder.

GAD = generalized anxiety disorder.

Finally, there may be influences associated with sleep architecture that may contribute to psychiatric disorder. A recent meta-analysis of sleep studies in PTSD found that lighter sleep (stage 1) and greater REM density distinguished PTSD from control participants. Further, fragmented REM sleep shortly after trauma is associated with PTSD.²⁶ REM sleep may be relevant for posttraumatic disorders because animal models posit that REM is related to emotional memory consolidation.²⁷ Interestingly, this has led to some (untested) speculation that sleep deprivation may be protective of subsequent posttraumatic disorders.²⁸ More recently, sleep deprivation has been found to limit generalization of extinction learning in humans.²⁹ Extinction learning refers to the new learning that a threat is passed and potential reminders no longer signal danger.³⁰ Although differences between sleep deprivation and sleep disturbance temper the inferences drawn from sleep deprivation studies,³¹ it is possible that sleep disturbance prior to trauma may lead to some degree of sleep deprivation after the traumatic event, and this may restrict extinction learning that is posited to be central to adaptation after a traumatic event. There is fMRI evidence of increased amygdala activation and reduced amygdala-medial prefrontal (mPFC) functional connectivity in response to emotional stimuli after sleep deprivation.³² These regions are pivotal to extinction learning,30 and so sleep disturbance may interfere with neural structures underpinning adaptation to trauma. It is important to note, however, that the state of evidence for the mechanisms of sleep disturbance, including the role of impaired REM, is very limited at this stage, and these suggestions are very speculative. We also note that the relationship between sleep disturbance and other disorders may involve a range of different mechanisms. For example, we note that sleep disturbance is linked to increased cortisol, 33,34 which is commonly associated with depressive disorders. Increased cortisol at the time of a traumatic event may cause one to be more vulnerable to the development of depression.

It is worth noting that a significant proportion of participants in this study (58%) had suffered a psychiatric disorder at some time in their lives prior to the injury. This raises the possibility that prior psychiatric disorder, and possibly sleep impairment, may contribute to the occurrence of traumatic injuries. We have previously reported from this data that the lifetime prevalence of psychiatric disorder in this cohort is higher than Australian norms, suggesting that occurrence of traumatic injury may be associated with prior psychiatric disorder.³⁵ This finding concurs with prior evidence that traumatic injury is associated with previous substance use³⁶ and previous psychiatric disorder.³⁷ It is also possible that sleep disturbance directly contributed to traumatic injury because of fatigue, impaired concentration, slowed reaction times, or other factors associated with sleep disturbance.³⁸ Unfortunately, our design did not allow us to index the causal role of sleep impairment on injury because we had no control condition without injury.

We recognize several limitations that suggest caution in interpretation of the current findings. First, we assessed sleep disturbance with a modified version of the SII, and so we were not able to confidently identify clinical insomnia prior to the traumatic injury. Second, although we indexed prior psychiatric disorder, we did not index lifetime sleep disturbance; we recognize that prior sleep disturbance that is either comorbid

with or independent of psychiatric disorder or subsyndromal psychiatric disorder may affect subsequent psychological functioning. The finding that the relationship between prior sleep disturbance and subsequent disorder was weaker when patients with prior disorder were included in the analyses supports the conclusion that there may be a complex relationship between prior psychological functioning, sleep disturbance, and adjustment to trauma. Third, all sleep pattern reports were collected retrospectively, and accordingly are subject to mood bias recollection.³⁹ Fourth, we were unable to index the quality or type of treatment received by patients, and accordingly could not assess its potential impact on adjustment.

These limitations notwithstanding, these data provide evidence that sleep deficits immediately prior to trauma exposure represent a marked risk factor for psychiatric disorder. It is interesting to consider these findings in the context of evidence that sleep impairment immediately after trauma exposure is a predictor of subsequent PTSD. 40,41 There is also much evidence that posttraumatic disorders, such as PTSD, are characterized by marked sleep dysfunction, with up to 91% of veterans with PTSD reporting sleep difficulties. 42 Further, there is some evidence that people with PTSD have poorer sleep efficiency and more awakenings than those without PTSD. 43 The current data raise an interesting question concerning the extent to which these sleep difficulties associated with PTSD are simply a function of PTSD symptoms or if they are predisposing problems that render people vulnerable to PTSD development.

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