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Early-life trauma is associated with rapid eye movement sleep fragmentation among military veterans

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Abstract

The role of sleep in the relations between early-life trauma and the development of adverse psychological trajectories is relatively unknown and was the primary aim of the present study. Military veterans were evaluated for Posttraumatic Stress Disorder, combat exposure, trauma history, sleep quality, disruptive nocturnal behaviors, and a subsample completed overnight polysomnography that yielded objectively measured sleep parameters. When relevant variables were controlled, increased earlier-life traumatic event exposure was associated with increased rapid-eye-movement sleep (REMs) fragmentation, and increased REMs fragmentation was associated with increased later-life disruptive nocturnal behaviors. REMs fragmentation carried an indirect relation between earlier-life trauma and later-life disruptive nocturnal behaviors. Objectively measured sleep parameters were used to describe REMs fragmentation physiology. The current findings elucidate the important role that earlier-life trauma exposure may have in the development of REM sleep physiology, and how this altered sleep physiology may have dynamic influences on subsequent posttraumatic stress symptoms in adulthood.

Keywords

Sleep; Development; Translational; Trauma; Fear; PTSD; Combat

INTRODUCTION

Early-life stress can be innocuous and may potentially enhance resilience to subsequent stressors (Lyons et al., 2010); however, timing of exposure during development, frequency of occurrence, intensity of the stressor, and prior experience(s) with adversity formulate a concoction that influences differential reactions to stress in later-life (Lupien et al., 2009). Approximately two-thirds of children experience a traumatic event (Centers for Disease Control and Prevention, 2010; Copeland et al., 2007), and 13.4% of them develop post-traumatic stress symptoms (Copeland et al., 2007). During early adulthood childhood trauma is associated with increased suicide attempts (Lipschitz et al., 1999; Johnson et al., 2002), illicit drug use and drug-related problems (Huang et al., 2011), arrest and violent offenses (Smith et al., 2005), rates of eating disorders (Kong & Bernstein, 2009), rates of depression (Chapman et al., 2004; Wiersma et al., 2009), and other various psychopathologies (Briggs-

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Gowan et al., 2010). Therefore, the identification of mechanisms that drive the relations between early-life trauma and the development of various psychopathologies is pertinent to inform prevention and intervention strategies targeted to buffer against adverse psychiatric trajectories among individuals exposed to trauma during early-life. The current study consisted of three aims to examine sleep as a potential mechanism that influences the relations between early-life trauma and later-life trauma associated adversities.

Sleep is a physiological mechanism that influences and is influenced by most aspects of brain physiology and waking behavior (Hobson, 2005; Siegel, 2005). A growing literature base and converging evidence has shown that among adults, sleep disturbance appears to be both a predisposing (Bryant, Creamer, O'Donnell, Silove, & McFarlane, 2010; Koren, Arnon, Lavie, & Klein, 2002) and perpetuating (Spoormaker et al., in press; also, see review [Mellman & Hipolito, 2006]) factor in the development of Post-Traumatic Stress Disorder (PTSD), as well as other trauma-associated adversities (see review [Germain et al., 2008]). Among adults, REM sleep disturbance appears to characterize and contribute to the pathogenesis of PTSD (Kobayashi et al., 2007; Ross et al., 1994a; Ross et al., 1989). For instance, within one-month of trauma exposure, a fragmented REM sleep profile was associated with the development of PTSD symptoms (Mellman et al., 2002). Similarly, heightened REM sleep fragmentation profiles have been detected among adults who had a longer latency (≤ 5 years) from trauma exposure (Breslau et al., 2004), and has been detected among combat-exposed military veterans (Mellman et al., 1995; Mellman et al., 1997; Ross et al., 1994b; Ross et al., 1994a). REM sleep disturbance subsequent to trauma exposure is particularly problematic because it is associated with dysfunction in emotional memory processing (Nishida, Pearsall, Buckner, & Walker; also, see reviews [Stickgold, 2002; Walker & van der Helm, 2009]), increased trauma-related nightmares (Habukawa et al., 2007), and impairments of conditioned fear extinction (Spoormaker et al., 2010). The neurobiological underpinnings of sleep disturbance within the PTSD condition are becoming better understood (see review [Germain et al., 2008]), which has contributed to the development of efficacious sleep focused PTSD treatments (see review [Nappi, Drummond, & Hall, 2012]). Although sleep is a treatment target among adults who suffer from PTSD, the role of sleep in the relations between early-life trauma and the development of subsequent adverse psychological trajectories is relatively unknown. Thus, the first aim of the present study was to identify whether earlier-life trauma exposure was associated with later-life REM sleep disturbances, sleep quality, disruptive nocturnal behaviors, and daytime PTSD symptoms.

A conceptual model has been proposed that identifies sleep as a mediator among the relations between childhood trauma exposure and subsequent negative health and behavioral outcomes during childhood (Spilsbury, 2009). Early-life trauma-associated sleep disturbances may also lead to psychopathologies in later-life. For instance, abused children demonstrate more difficulty initiating sleep and have twice as many nocturnal arousals than nonabused control children (Glod et al., 1997a; Glod et al., 1997b). Furthermore, longitudinal work indicated that sleep disturbances during childhood predict the development of anxiety disorders during adulthood (Gregory et al., 2005). Therefore, early-life trauma-associated sleep disturbances may contribute to and perpetuate subsequent adverse psychological conditions in later-life. Thus, the second aim of the present study was to evaluate the role that earlier-life trauma associated REM sleep disturbance may have in the pathogenesis of later-life trauma associated adversities.

Early-life trauma is likely to have a long-term effect on sleep physiology. Accordingly, retrospective studies indicate that parental emotional abuse during childhood is associated with worsened sleep quality during older-adulthood (Poon & Knight, 2011), and similarly among primary insomniacs, early-life trauma exposure is associated with more nocturnal

arousals during sleep in later-life (Bader et al., 2007a; Bader et al., 2007b). Along this line, experimental animal models have been developed to better understand human PTSD associated sleep disturbances (Pawlyk et al., 2005; Jha et al., 2005). These models have been applied to further elucidate the long-term effects that fear conditioning may have on subsequent sleep physiology. Specifically, fourteen days after male Sprague-Dawley rats were conditioned to fear a stimulus, reexposure to the conditioned stimulus elicited significant alterations to REM sleep microarchitecture, which included increased fragmentation and increased myoclonic twitch density (Madan et al., 2008). Early-life trauma may therefore have a long-term impact on sleep physiology that is specific to the REM sleep profile. Thus, the third aim of the present study was to examine aspects of REM sleep physiology that may contribute to REM sleep disturbances.

METHODS AND MATERIALS

The current study is a secondary data analysis of projects that examined sleep treatments among military veterans (R34 MH-080696-01, R21 MH-083035-01, PR054093, and PT073961). Sleep treatments were focused to decrease insomnia and nightmares, and to generally increase sleep quality; treatments included brief behavioral treatment for insomnia, prazosin administration, and a behavioral sleep intervention. All studies had several overlapping measures during the initial study visit. All projects were approved by the institutional review board at the University of Pittsburgh and the Human Research Protection Office of the Department of Defense. Informed consent and Health Information Portability and Accountability Act authorization were obtained from all participants prior to the study procedures.

Participants

Participants were $N = 63$ military veterans who were recruited from community advertisements (e.g. local television commercials, radio commercials, bus signs, list-serves, flyers) for the larger projects that examined sleep neurobiology and treatments for sleep difficulties experienced by military veterans. Participants were free of current (past six months) major depression, suicidality, substance or alcohol abuse, and psychotic or bipolar disorder (lifetime). Participants with an apnea-hypopnea index ≥ 15 and periodic limb movement disorder (PLMD; index and arousal ≥ 10) were not included in the study. Participants were included in the present study if they were administered at least two measures used in the current analyses. All participants were administered the Structured Clinical Interview for DSM-IV Axis I Disorders (First et al., 1995) and were primarily diagnosed with PTSD (57.14%), insomnia (23.81%), or had an otherwise specified disorder (4.76%); a portion of participants were healthy controls (14.29%). Participants served in the Army (82.54%), Marines (7.94%), Navy (6.35%), and Air Force (3.18%). Participants were deployed to combat theatres that included Operation Iraq/Enduring Freedom (57.14%), Persian Gulf War (14.29%), Vietnam (11.11%), a different engagement (4.76%), or no combat-exposure (12.70%).

Measures

Clinician-Administered PTSD Scale—The Clinician-Administered PTSD Scale (CAPS) was used to determine daytime PTSD symptomatology (Blake et al., 1990). The CAPS is a structured interview that examines frequency and intensity of core PTSD symptoms and is used to identify the presence, absence, and severity of PTSD symptomatology. The two sleep items were removed (i.e. “Difficulty falling or staying asleep,” and “Nightmares”) to avoid multicollinearity with other sleep variables during analyses.

Combat Exposure Scale—The Combat Exposure Scale (CES) was used to determine combat exposure severity (Keane et al., 1989). The CES is a self-report measure that comprises seven likert items that describe severity of combat experience, each scaled from one (No) to five (≥ 51 times). The total CES score can range from 0 (less combat exposure) to 41 (more combat exposure). The CES has good internal consistency Cronbach's $\alpha = .85$, test-retest reliability $r = .97$, and previously discriminated ($p < .005$) between PTSD and non-PTSD combat-exposed veterans.

Pittsburgh Sleep Quality Index—The Pittsburgh Sleep Quality Index (PSQI) was used to determine sleep quality from the previous month (Buysse et al., 1989). The PSQI is comprised of 19 items that yield seven component scores; component scores are summed to create a total score. The total score can range from 0 (better) to 21 (worse), and scores ≤ 5 are associated with good sleep quality whereas scores > 5 are associated with poor sleep quality. The PSQI has a sensitivity and specificity of 89.6% and 86.5% respectively (Buysse et al., 1989).

Pittsburgh Sleep Quality Index-Addendum for PTSD—The PSQI-Addendum (PSQI-A) was used to determine PTSD associated disruptive nocturnal behaviors that are hallmark to PTSD (Germain et al., 2005). The PSQI-A identifies the frequency of seven different sleep disturbances to create a total score. Examples of specific sleep disturbances assessed with the PSQI-A include; hot flashes, memories or nightmares of the traumatic experience, and episodes of terror during sleep. The total score can range from 0 (normal) to 21 (severe), and scores ≥ 4 can be used to discriminate participants with, from those without, PTSD. The PSQI-A has a sensitivity and specificity of 94% and 82% respectively (Germain et al., 2005).

Trauma History Questionnaire—The Trauma History Questionnaire (THQ) was used to retrospectively identify earlier-life and later-life trauma histories (Green, 1996). The THQ contains four event categories: “Crime Related Events” contains four discrete items; “General Disaster and Trauma” contains 13 discrete items; “Physical and Sexual Experiences” contains six discrete items; and “Other events” contains one item that for any extraordinarily stressful situation that was not included in the other categories. The number of discrete traumatic events experienced before age 18 were summed to indicate earlier-life trauma exposure. Likewise, the number of discrete traumatic events experienced during or after age 18 were summed to indicate later-life trauma exposure; later-life trauma also included traumas associated with combat exposure.

Overnight polysomnography—The PSG montage included bilateral central and occipital electroencephalography (EEG) channels, electro-oculogram, submentalis electromyogram, and electrocardiogram. EEG signals were recorded at 20-second epochs, were digitized at 256 Hz, decimated to 128 Hz, and sleep stages were visually scored according to Rechtschaffen and Kales criteria (Brunner et al., 1996; Vasko et al., 1997; Rechtschaffen & Kales, 1968). The REM sleep measures that were examined included REM latency, % REM, number of REM periods, REM fragmentation, and REM microarousals. Given the centrality of REM fragmentation to the current work (as described below), the variable was defined as “The number of occurrences of consecutive epochs scored as wake and/or NREM within REM periods immediately preceded by, and followed by, an epoch of REM.”; all other REM sleep measure definitions are provided in S1. To further profile REM fragmentation, sleep stage transitions during REM periods were examined. Quantitative EEG (qEEG) measures included average relative power in Delta (.5-4 Hz) and Beta (16-32 Hz) bands during REM sleep; qEEG procedures are provided in S2.

Procedure

During the initial study visit participants self-administered the PSQI, the PSQI-A, and the THQ; additionally, participants were administered the CAPS by a clinician. All participants ($N = 63$) from the larger projects had overnight polysomnography (PSG) sleep studies; see Table 1 for demographic information. Participants were administered three consecutive overnight polysomnography (PSG) sleep studies at the Neuroscience Clinical and Translational Research Center (N-CTRC) at the Western Psychiatric Institute and Clinic. The first PSG night was an accommodation and sleep disorder (i.e. sleep disordered breathing and PLMD) screening night that was not used for further analyses. The two consecutive PSG sleep study nights that followed the accommodation and screening night were considered baseline nights for the larger projects; these were considered the study nights for the current analyses. Sleep data from these two study nights were averaged to provide stable measures. The PSG sleep studies were independently scored by Registered Sleep Technologists within the N-CTRC who were blind to participants' clinical status.

Statistical Analyses

SPSS 18.0 (SPSS Inc, Chicago, IL) was used for statistical calculations; a $p < 0.05$ was considered statistically significant. Descriptive statistics were calculated for demographic, as well as sleep and PTSD measures. Separate partial correlations were calculated for earlier-life (covariates: age at THQ completion, CES, later-life trauma) and later-life trauma (covariates: age at THQ completion, earlier-life trauma) to examine their relations with daytime PTSD severity, disruptive nocturnal behaviors, sleep quality, and objective sleep measures (i.e. PSG, qEEG). Age at THQ completion was included as a covariate for all comparisons because latency from a traumatic experience to the age at THQ completion could have influenced salience of early-life and later-life traumatic event recall. Additionally, to permit analyses of each variable's distinctive correlates, CES and later-life trauma were also included as covariates for the earlier-life trauma comparisons; whereas, earlier-life trauma was included as a covariate for the later-life trauma comparisons.

A Sobel test for mediation (Sobel) was calculated with a JavaScript program (Preacher & Leonardelli, 2010) to examine the potential indirect associations among earlier-life trauma exposure with daytime PTSD severity, disruptive nocturnal behaviors, and sleep quality while accounting for REM sleep disturbance. Results from a Monte Carlo study of 14 different mediation techniques, that are used to test path models across various disciplines, indicated that the Sobel test is the preferred technique to examine mediation (MacKinnon et al., 2002). A benefit of the Sobel technique is its ability to uniquely provide a significance test to examine the indirect effect of an independent variable on a dependent variable by means of an intervening variable (Preacher & Hayes, 2004).

A stepwise linear regression was calculated to examine which REM sleep variable(s) accounted for the most variance in REM sleep fragmentation. REM sleep variables examined included percentage of wake during REM periods, percentage of non-REM (NREM) during REM periods, and frequency of micro arousals during REM sleep. A stepwise regression was calculated because this analysis was used to explore variables associated with REM sleep fragmentation and no a-priori hypothesis was made. Bivariate correlations were calculated to examine relations between REM sleep fragmentation and average relative power in delta and beta bands during REM sleep.

RESULTS

Participant demographic information and descriptive data are indicated in Table 1. Detailed THQ descriptive data are indicated in Table 2. Descriptive statistics for visually scored PSG and qEEG variables are indicated in Table 3.

Following the PSG adaptation and screening night, a portion of participants had one subsequent PSG study night ($n = 15$); whereas, the remaining participants had two subsequent PSG study nights ($n = 47$)—which were averaged for stability. To examine possible group differences due to the study procedures, REM sleep variables were compared between participants who had one study night and participants who had two study nights. Participants did not differ on REM fragmentation, total percent REM, or number of REM periods. However, participants who had one study night had longer REM latency than participants who had two study nights ([102.31 min, 74.01 min, respectively] $F [1, 61] = 5.57, p = .02, g = .69$). Participant apnea-hypopnea index was not associated with REM latency ($r = -.10, p = .45$), % REM ($r = -.09, p = .48$), number of REM periods ($r = -.05, p = .69$), REM fragmentation ($r = -.21, p = .11$), or REM microarousals ($r = .003, p = .98$); all comparisons were made with a one-tailed significance test.

The relations among earlier-life trauma, and for comparative purposes later-life trauma, with sleep and PTSD associated behaviors during adulthood were examined while controlling for relevant covariates. Associations among earlier-life and later-life traumas with study variables are indicated in Table 4. Increased earlier-life trauma was significantly associated with increased REM sleep fragmentation, and later-life trauma—respectively by correlation strength. Increased later-life trauma was associated with increased PTSD severity and disruptive nocturnal behaviors—respectively by correlation strength. Higher PTSD severity was significantly associated with higher disruptive nocturnal behaviors ($r = .60, p < .001$) and lower sleep quality ($r = .25, p = .03$). Earlier-life trauma associated REM sleep fragmentation was examined further; an example of REM sleep fragmentation is demonstrated in Figure 1.

The impact of earlier-life trauma associated REM sleep disturbances in the development and pathogenesis of PTSD symptomatology during adulthood was examined. Earlier-life trauma was associated with REM sleep fragmentation when controlling for age, later-life trauma, and CES ($t = 2.93, p = .005; B = .99, SE = .34$). REM sleep fragmentation was associated with disruptive nocturnal behaviors ($t = 2.91, p = .005; B = .30, SE = .10$). When accounting for REM sleep fragmentation, there was an indirect relation between earlier-life trauma and disruptive nocturnal behaviors (Sobel = 2.08, $SE = .14, p = .04$). REM sleep fragmentation was not associated with sleep quality ($t = 1.64, p = .11; B = .21, SE = .13$), or PTSD severity ($t = 1.11, p = .27; B = .72, SE = .65$); therefore, indirect relations among earlier-life trauma and these variables were not examined.

REM sleep physiology that may contribute to REM sleep fragmentation was examined in further detail. Percentage of NREM sleep during a REM sleep period ($\beta = .45$), percentage of wake during a REM sleep period ($\beta = .40$), and total frequency of micro arousals during REM sleep ($\beta = .33$) were associated with REM sleep fragmentation ($R^2 = .50, F [3, 59] = 19.88, p < 0.001$), respectively; examples of each variable during a REM period is demonstrated in Figure 2. Furthermore, average relative power in delta ($r = -.26, p = .049$) and beta ($r = .26, p = .049$) bands during REM sleep were each significantly associated with REM sleep fragmentation.

DISCUSSION

The present study identified independent relations among earlier-life trauma exposure and REM sleep fragmentation during adulthood. The current findings elucidate the important role that earlier-life trauma exposure may have in the development of REM sleep physiology, and how this altered sleep physiology may have dynamic influences on subsequent PTSD associated symptoms, such as disruptive nocturnal behaviors. Furthermore, the REM sleep fragmentation profile was described with visually scored, as well as quantitative EEG measures. The confluence of the current findings can extend existing psychobiological models (see: [Germain et al., 2008; Spilsbury, 2009]) by providing insight into early-life experience and REM sleep physiology. These models may ultimately be used to predict the developmental course of psychiatric adversities subsequent to trauma, and may provide insight into timing for early intervention.

The independent relations among earlier-life trauma with sleep and PTSD associated behaviors during adulthood were calculated; there were striking associations between earlier-life trauma and REM sleep fragmentation during adulthood. Previous work has identified more proximal associations between trauma exposure, and REM sleep disturbance among humans (Habukawa et al., 2007; Mellman et al., 2002), also replicated in the current study; however, the current work demonstrates the prolonged influence that earlier-life trauma may have on the development of REM sleep physiology. This finding replicates, and thus translates to humans, similar findings previously described by experimental animal models that identified the prolonged effect that fear-conditioning has on sleep physiology (DaSilva et al., 2011; Madan et al., 2008). Furthermore, earlier-life trauma was independently associated with REM sleep fragmentation whereas later-life trauma was limited to a non-significant trend. This particular finding provides insight into the interaction between early-development and adverse early-life experiences, which may have a salient effect on developmental trajectories of sleep physiology. This finding does not discount the relation between REM sleep fragmentation and later-life trauma since the non-significant association was likely due to low statistical power.

The unique relation between earlier-life trauma and fragmented REM sleep in the pathogenesis of PTSD symptomatology necessitated further examination. Additional analyses identified that REM sleep fragmentation carried an indirect association between earlier-life trauma and disruptive nocturnal behaviors that are characteristic to PTSD. Disruptive nocturnal behaviors, measured by the PSQI-A, have predictive validity in discriminating individuals with and without PTSD (Germain et al., 2005) and were in fact associated with daytime PTSD severity symptoms among the current sample. REM sleep fragmentation associated with earlier-life trauma may have pervasive influences on subjective sleep quality in adulthood. These pervasive influences could potentially propagate the discrepancies found between subjective and objective sleep measures among individuals who suffer from PTSD (e.g. references [Klein et al., 2003; Dagan et al., 1997; Kobayashi et al., 2007]). Thus, earlier-life trauma associated REM sleep fragmentation may increase vulnerability to psychopathologies in adulthood, especially among military veterans.

Study results guided a further dissection of REM sleep fragmentation that provided a detailed analysis and description of its profile. Visually scored EEG data were examined to better understand the REM fragmentation profile. REM sleep fragmentation was most strongly associated with non-REM during a REM sleep period, wake during a REM sleep period, and micro arousals during REM sleep, respectively. Recent work has demonstrated that these micro-level sleep stage transitions can predict subjective sleep quality over-and-beyond commonly used sleep architecture measures, and can be used to more intricately understand sleep continuity (Laffan et al., 2010). QEEG calculations during REMs indicated

that REMs fragmentation was associated with decreased qEEG delta and increased qEEG beta bands. These results are congruent with previous work that identified self-reported psychological stress as associated with decreased qEEG delta and increased qEEG beta bands during non-REM sleep among insomniacs (Hall et al., 2007). Although previous work has examined qEEG among military veterans to identify a neurobiological basis for PTSD (e.g. references [Begic et al., 2001; Jokic-Begic & Begic, 2003; Woodward et al., 2000]), the current results provide the initial qEEG report on the physiology of REM sleep in relation to earlier-life trauma associated REM sleep fragmentation.

During early-life, changes in sleep and brain development are drastic and are sensitive to peripheral factors such as stress (Perry et al., 1995); thus, early-life trauma may have a long-term effect on sleep physiology. Separate research areas indicate that trauma can permanently alter the hypothalamic-pituitary-adrenal axis physiology among children (Neigh et al., 2009) and normal developmental changes in sleep physiology are most pronounced during early-life (Iglowstein et al., 2003; McLaughlin & Williams, 2009; Ohayon et al., 2004). For instance, the natural developmental decrease in REMs during early-life coincides with a high volume of neurological changes, including a decrease in noradrenergic inhibition (see review [Garcia-Rill, Charlesworth, Heister, Ye, & Hayar, 2008]). A body of work conducted by Mellman and colleagues has indicated that noradrenergic hyperactivity, possibly due to lack of noradrenergic inhibition, during REM sleep may lead to REM sleep disturbance, which appears to be central to the development of PTSD (Ross et al., 1989; also, see review [Mellman & Hipolito, 2006]). Decreased noradrenergic tone is thought to be the primary mechanism underlying the efficacy of prazosin, a α -1 adrenergic antagonist, to treat nightmares and sleep disturbances that are associated with PTSD (Raskind et al., 2003; Raskind et al., 2007). When synthesized with the current results, traumatic events that occur during earlier-life, in sequence with normal developmental changes in sleep physiology, may permanently alter noradrenergic regulation and REM sleep physiology, thus resulting in life-long REMs disturbances as described by Garcia-Rill and colleagues (2008). This interpretation is congruent with previous longitudinal work that identified a strong association between adverse early-life experiences and poor self-reported sleep quality in adulthood (Koskenvuo et al., 2010). However, further research is necessary to identify the effects of timing, frequency, intensity, and contexts of trauma exposure during early-life on specific developmental features of sleep physiology, especially REM sleep.

Evidence continues to build to support the function of sleep, and particularly REM sleep, in the process of memory consolidation (see review [Stickgold & Walker, 2005]). REM sleep and memory have direct implications for emotional memory processing that are fundamental to various stress-related psychopathologies including PTSD. A 'sleep to *forget* and sleep to *remember* hypothesis' has been postulated and highlights the role that REM sleep disturbance has in emotional memory processing, that when present, can initiate and maintain mood disturbances (Walker & van der Helm, 2009). The current findings support this hypothesis, and together direct future research to identify mechanisms that reveal the relations between early-life trauma, REM sleep physiology, and emotional memory processing.

Recent research has sought to identify various genetic and transgenerational mechanisms that influence adverse reactions to early-life traumatic experiences. A large epidemiological study identified that childhood maltreatment predicted later-life depression only among individuals who possessed a short 's' allele in the 5-HTT gene-linked polymorphic region; additionally, these individuals were more likely to demonstrate adverse psychiatric reactions to stressful life events compared to individuals who did not have the long allele (Caspi et al., 2003). Furthermore, increased methylation has been shown to result from early-life

adversity (Beach et al., 2010) and appears to moderate the relation between the 5-HTT polymorphism and adverse psychiatric reactions to stress; thus, identifying an epigenetic gene-by-environment interaction (van IJzendoorn et al., 2010). Additionally, early-life stress can also have a transgenerational effect on subsequent generations that did not directly experience the stressor. For example, male mice who received a salient stressor during postnatal days 1-14, as well as their offspring who did not receive the stressor, demonstrated methylation changes and depressive-like behaviors compared to control mice (Franklin et al., 2010). Thus, the search for early-life stress related mechanisms that lead to adverse developmental and psychiatric trajectories are at the forefront of science. Future research can be deeply enriched by further examining the novel contributions that REM sleep physiology has among these adverse trajectories. Furthermore, REM sleep physiology may be a viable and non-invasive biomarker to detect the pathogenesis of PTSD development, or susceptibility, following trauma exposure (e.g. Mellman & Hipolito, 2006).

All of the current findings were in their expected directions, were identified despite relevant control variables, and aggregated together to bolster the study interpretations. Nevertheless, methodological limitations need to be considered when interpreting results from the current study. The current sample was assembled out of convenience from multiple studies, which limited the research design to a cross-sectional analysis without a control group. Following the sleep disorders screening and adaptation night, 23.81% of participants were administered one PSG study night whereas the remainder were administered two PSG study nights. Participants who were administered one study night had longer REM sleep latency than those who were administered two study nights; however, the two groups did not differ on any other REMs variable. Subtle differences in REM sleep values can be expected. Previous research among military veterans with PTSD indicated that participants demonstrated higher REMs density during the first PSG night compared to their second PSG night (Ross et al., 1999). Furthermore, previous work among healthy community based participants has indicated that the first-night effect during ambulatory PSG can extend beyond one night (Le Bon et al., 2001)—a methodological limitation that can impact a majority of PSG sleep research studies. Nevertheless, the primary study variable, REM sleep fragmentation, did not differ as a function of the number of PSG study nights. As expected, the sample demonstrated high daytime PTSD severity, poor sleep quality, and high disruptive nocturnal behavior prevalence. The CAPS scores may appear low for the particular sample; however, a conservative analytic approach was taken to remove the sleep item scores from the CAPS.

In order to utilize the most accurate amount of data from the THQ, trauma history was limited to the report of discrete events experienced during earlier-life and later-life. Age during each traumatic event was not examined because some participants chose not to provide that level of detail in response to some questions, but rather provided an age range. However, the correlation between later-life trauma with the CAPS (gold-standard) demonstrated the effectiveness of the THQ. Furthermore, the prevalence rate of 65.08% who experienced at least one earlier-life traumatic event is consistent with data from the Center for Disease Control, indicating that two thirds of the general population report childhood adverse events (Centers for Disease Control and Prevention, 2010). Later-life trauma was associated with daytime PTSD severity and disruptive nocturnal behaviors, which was anticipated because these particular traumatic events are the expected antecedents to PTSD severity and symptoms. The association between earlier-life and later-life trauma was also anticipated because early-life trauma exposure is associated with a higher propensity for re-exposure to trauma (Widom et al., 2008). Contrary to expectations, there was not a significant association between earlier-life trauma and daytime PTSD severity. The relation between earlier-life trauma and daytime PTSD severity may have been influenced by the retrospective study design, lack of the trauma measurement sensitivity, or the high experience of later-life trauma that may have overshadowed the recollection of earlier-life

traumas. When appropriate, future research should utilize prospective designs, a multidimensional assessment battery to probe trauma exposure, and diverse samples to better identify the etiology and effects of earlier-life trauma (e.g. Bernstein et al., 1994; Briere, 1996).

Although a convenience sample was utilized, military veterans are an enriched population to examine post-trauma REM sleep disturbances due to their high-risk for trauma exposure and high rates of PTSD (Hoge et al., 2004; RAND, 2008). Knowledge accrued from military samples can be specifically utilized to help identify basic physiological mechanisms that result from trauma-exposure and that contribute to adverse psychiatric conditions. Additionally, such physiological results can be applied to detect signals of trauma-related adversities that may be expressed more subtly among other high-risk civilian populations, such as public service employees (e.g. police officers, firefighters, emergency medical technicians), victims of violence (e.g. rape, physical assaults, terroristic attacks), and individuals who suffer from the aftermath of natural disasters (e.g. hurricanes, tornados, wildfires, floods, tsunamis).

Conclusion

The current study suggests that among the military population, early-life trauma may affect the development of REM sleep physiology and can be applied to better understand the role of REM sleep in context of trauma associated psychological conditions including PTSD. More broadly, the potential impact of early-life trauma exposure on REM sleep may provide novel insight into biological mechanisms, such as the processing of emotional memories and HPA axis modification, for stress resilience that can be modifiable targets for intervention. Currently, efficacious sleep treatments are being implemented to treat persons who suffer from PTSD (see review [Nappi et al., 2012]). The present study can be used as preliminary evidence to initiate sleep monitoring, promote sleep preservation, or implement sleep treatment subsequent to early-life trauma exposure despite the clinical expression. These practices could be considered as preventative measures to help preserve healthy REM sleep, and buffer against adverse processing of emotional memories, which may lead to psychopathological vulnerabilities in later-life. Cumulatively, the current work provides novel insights into early-life trauma, which may be applied to inform prevention strategies to improve functional outcomes and potentially correct adverse developmental trajectories among trauma exposed individuals.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Earlier-life trauma was associated with later-life REM sleep fragmentation (REMs_f).
- REMs_f carried an indirect relation among early-life trauma and later-life sleep.
- The REMs_f physiological profile was described with EEG and qEEG sleep measures.
- Dynamic relations may exist among early-life trauma, sleep, and psychopathology.

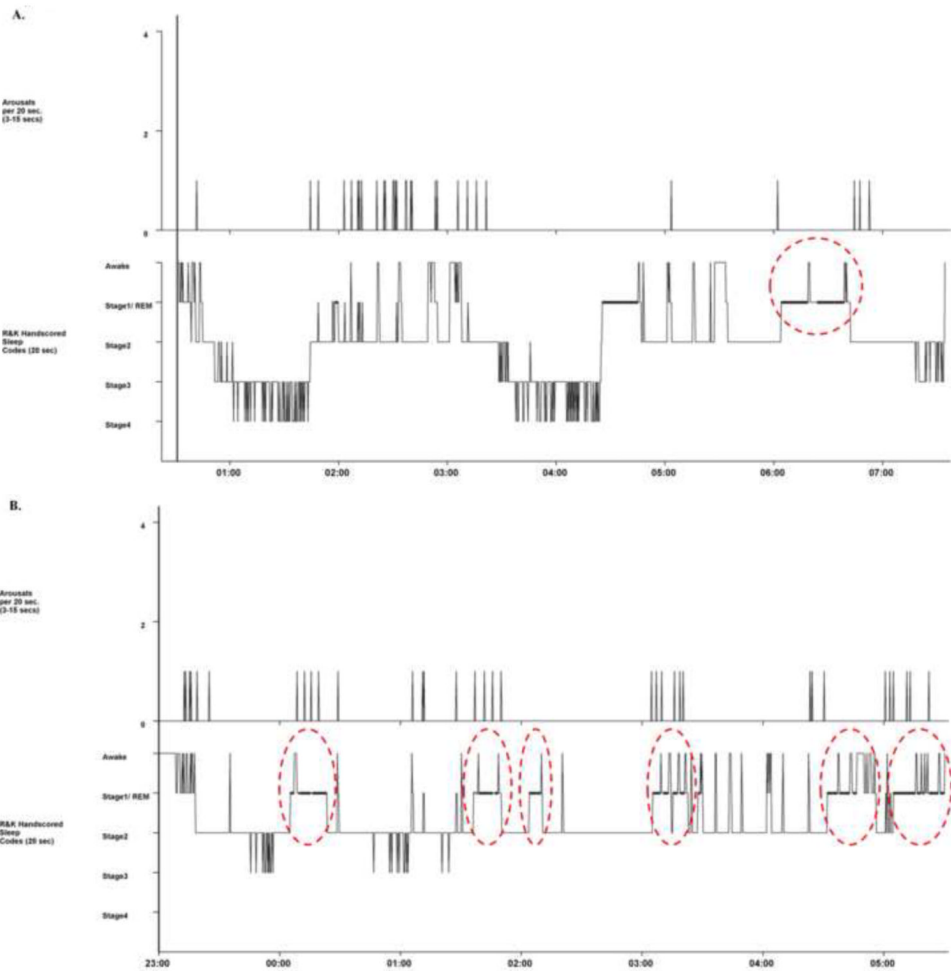


Figure 1. Selected sleep hypnograms that depict low and high REM sleep fragmentation (i.e. wake or NREM during a REM period), respectively. Clock time during the sleep study is represented on the X-axis; sleep stages scored according to Rechtschaffen and Kales (1968) criteria are indicated on the lower y-axis, and microarousals are indicated on the upper y-axis. Examples of sleep fragmentation are circled.

A. Low REM sleep fragmentation value = 1: 30 year-old White male without PTSD (Control) who had 0 early-life and 1 later-life traumatic events.

B. High REM sleep fragmentation value = 16: 35 year-old White male with PTSD who had 3 early-life and 6 later-life traumatic events.

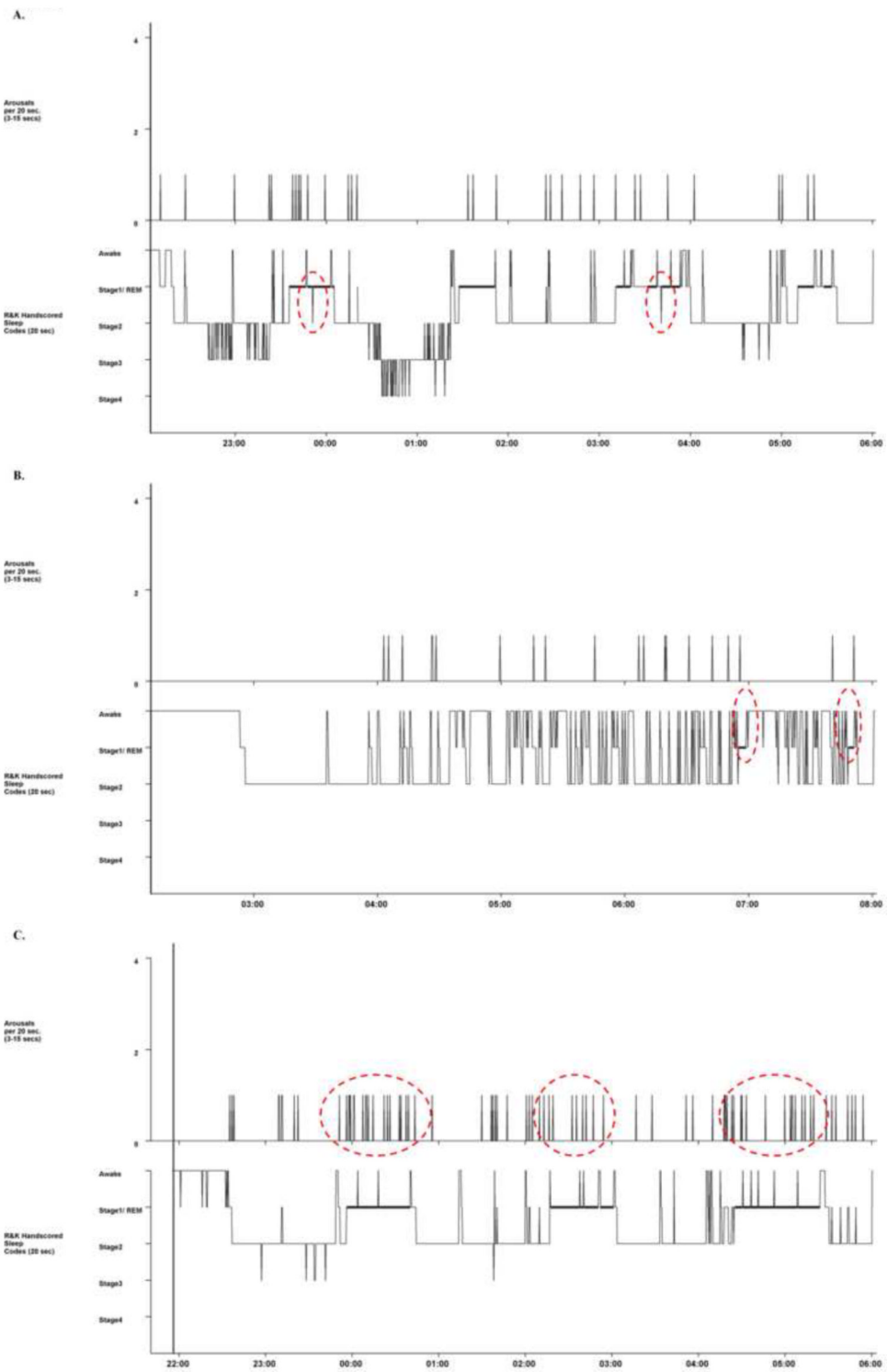


Figure 2. Selected sleep hypnograms that depict sleep state transitions that include REM to NREM, REM to wake, and micro arousals during REM, respectively. Clock time during the sleep study is represented on the X-axis; sleep stages scored according to Rechtschaffen and Kales

(1968) criteria are indicated on the lower y-axis, and microarousals are indicated on the upper y-axis. Examples of respective stage transitions and arousals are circled.

- A. Transition to NREM sleep during a REM sleep period: 32 year-old White male with PTSD who had 4 early-life and 9 later-life traumatic events.
- B. Transition to wake during a REM sleep period: 51 year-old African American male with PTSD who had 6 early-life and 9 later-life traumatic events.
- C. Micro arousals during REM sleep: 40 year-old White male with PTSD who had 1 early-life and 7 later-life traumatic events.

Table 1

Participant demographic information, descriptive data, and sub-sample comparisons

Variable	%
Male	90.48
White	84.13
African American	14.29
Other	1.59

Variable	<i>M</i>	<i>SD</i>
Age	39.25	13.09
CAPS total	27.71	19.67
CES	15.82	12.10
Early-life trauma	1.40	1.53
Later-life trauma	6.78	3.27
PSQI	9.39	4.21
PSQI-A	3.45	3.29

Note: g = Hedge's g effect size correction for unequal sample sizes. The two sleep items were removed from the CAPS. Early-life and later-life trauma indicate number of discrete traumas before, and after, 18 years-old respectively. There were no sex differences for early-life ($t [1, 134] = 1.46, p = .15$) or later-life trauma ($t [1, 134] = 1.31, p = .19$). Clinician-Administered PTSD Scale (CAPS), Pittsburgh Sleep Quality Index (PSQI), PSQI-Addendum for Post Traumatic Stress Disorder (PSQI-A).

Table 2

THQ descriptive data by category among participants ($N = 63$) who reported at least one trauma during earlier-life ($n = 41$), and among participants who reported at least one trauma during later-life ($n = 61$)

Variable	Earlier-life Trauma Variety	Later-life Trauma Variety
Endorsement of ≥ 1 Traumatic Event	65.08 %	96.83 %
Crime Related Events	26.83 %	34.43 %
General Disaster and Trauma	63.42 %	98.36 %
Physical and Sexual Experiences	48.78 %	34.43 %
Other Events	7.32 %	16.39 %

Table 3Participant descriptive statistics for visually scored sleep ($n = 63$) and qEEG variables ($n = 59$)

Variable	<i>M</i>	<i>SD</i>
Sleep Latency (min)	23.91	24.19
Total Sleep Time (min)	406.13	67.87
Wake After Sleep Onset (min)	44.12	36.52
Sleep Efficiency (%)	84.22	10.47
NREM %	75.45	4.82
Stage 1 %	5.73	3.37
Stage 2 %	64.18	7.01
Slow Wave Sleep %	5.52	5.99
REM %	24.56	4.81
Number of REM periods	3.54	1.00
REM fragmentation number	7.84	3.98
REM latency time (min)	80.75	41.99
*Delta in REM (0.5-4 Hz)	0.6034	0.0777
*Beta in REM (16-32 Hz)	0.0586	0.0355

Note. Only REMs variables were used in primary analyses.

Quantitative Electroencephalography (qEEG), Rapid Eye Movement Sleep (REM).

* indicates qEEG variables.

Table 4

Correlations among earlier-life trauma, later-life trauma, daytime PTSD severity, and subjective and objective sleep measures when controlling for relevant variables.

Variable	Earlier-life trauma [†]		Later-life trauma [‡]	
	df	r	df	r
Later-life trauma	60	.25	.048	-
CAPS total	56	.13	.34	.58
PSQI	55	.17	.21	.57
PSQI-A	54	.24	.07	.56
REM percent	57	.08	.57	.59
Number of REM periods	57	.02	.91	.59
REM fragmentation	57	.36	.005	.59
REM latency	57	-.13	.34	.59
*Delta in REM (0.5-4 Hz)	53	.09	.50	.55
*Beta in REM (16-32 Hz)	53	.08	.56	.55

Note.

No qEEG variable was associated with CAPS, PSQI, or PSQI-A. No other non-REM sleep variable indicated in Table 3 was associated with earlier-life, or later-life trauma. The two sleep items were removed from the CAPS. Quantitative Electroencephalography (qEEG), Clinician-Administered PTSD Scale (CAPS), Pittsburgh Sleep Quality Index (PSQI), PSQI-Addendum for Post Traumatic Stress Disorder (PSQI-A), Rapid Eye Movement Sleep (REM).

⁻ indicates statistics that were not calculated for comparisons

* indicates qEEG variables.

[†] indicates associations while controlling for age, CES, and later-life trauma (age was the only control variable in the earlier- and later-life trauma association).

[‡] indicates associations while controlling for age, and earlier-life trauma.