Title

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Journal

Journal of Sleep Research, 22(6)

ISSN

0962-1105

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Publication Date

2013-12-01

DOI

10.1111/jsr.12064

Peer reviewed

Published in final edited form as:
J Sleep Res. 2013 December ; 22(6): 679–687. doi:10.1111/jsr.12064.

SEX DIFFERENCES IN OBJECTIVE MEASURES OF SLEEP IN PTSD AND HEALTHY CONTROL SUBJECTS

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Summary

A growing literature shows prominent sex effects for risk for PTSD and associated medical comorbid burden. Prior research indicates that PTSD is associated with reduced slow wave sleep (SWS), which may have implications for overall health, and abnormalities in REM sleep, which have been implicated in specific PTSD symptoms, but most research has been conducted in male subjects. We therefore sought to compare objective measures of sleep in male and female PTSD subjects with age and sex-matched control subjects. We used a cross-sectional, 2×2 design (PTSD/control × female/male) involving 83 medically healthy, non-medicated adults aged 19–39 in the inpatient sleep laboratory. Visual analysis of EEG demonstrated that PTSD was associated with lower SWS duration ($F(3,82)=7.63$, $p=.007$) and SWS percent ($F(3,82)=6.11$, $p=.016$). There was also a group by sex interaction effect for REM duration ($F(3,82)=4.08$, $p=.047$) and REM percent ($F(3,82)=4.30$, $p=.041$), explained by greater REM sleep in PTSD females as compared to control females, a difference not seen in male subjects. Quantitative EEG analysis demonstrated that PTSD was associated with lower energy in the delta spectrum ($F(3,82)=6.79$, $p=.011$) in NREM sleep. SWS and delta findings were more pronounced in males. Removal of PTSD subjects with comorbid MDD, who had greater PTSD severity, strengthened delta effects but reduced REM effects to non-significance. These findings support prior evidence that PTSD is associated with impairment in the homeostatic function of sleep, especially in men with the disorder. These findings suggest that group by sex interaction effects on REM may occur with more severe PTSD or with PTSD comorbid with MDD.

Keywords

Polysomnography; PTSD; sex differences; quantitative EEG; Slow Wave Sleep; REM sleep

Introduction

Subjective sleep disturbance characterized by non-restorative sleep, frequent awakenings, and nightmares related to traumatic life events are core features of posttraumatic stress disorder (PTSD). Despite the prominence of these symptoms in the distress experience of PTSD patients, the underlying neurophysiology of disturbed sleep in PTSD is poorly understood (Spoormaker and Montgomery, 2008, Germain, 2012). Research to date has produced conflicting findings regarding differences in objective measures of sleep in PTSD subjects and healthy controls. Furthermore, because most studies of sleep in PTSD have

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None of the authors have any financial interests or conflicts of interest to report.

been conducted in male samples, very little is known about objective sleep disturbance in women with PTSD (Kobayashi et al., 2007).

A meta-analysis by Kobayashi and colleagues provides a synthesis of the available information on visually scored objective sleep disturbance in PTSD (Kobayashi et al., 2007). Based on a review of 20 polysomnographic studies of PTSD+ and PTSD− subjects conducted between 1966 and 2006, the authors determined that PTSD was associated with a statistically significant increase in Stage 1 sleep and a statistically significant decrease in SWS.

There is scant research on quantitative analysis of sleep EEG in PTSD and controls. However, a handful of studies have found that PTSD is associated with a decline in delta sleep, at least in male subjects (Otte et al., 2007, Neylan et al., 2003, Woodward et al., 2000, Neylan et al., 2006). For example, in a sample of male PTSD subjects and age-matched controls studied under controlled laboratory conditions, Neylan and colleagues demonstrated a significant decrease in delta sleep in PTSD subjects as compared to controls. Using similar methods, Otte and colleagues found a numerical, but non-significant decrease in delta sleep in female PTSD subjects as compared to controls (Otte et al., 2007). In contrast, a small in-home study examining delta sleep in PTSD in a mixed gender, but predominantly male sample, found increased delta sleep in PTSD (Germain et al., 2006). Because total slow wave (delta) activity is associated with the homeostatic recovery function for the organism and is increasingly demonstrated to have a pronounced role in glucose metabolism and other fundamental biological processes, deficiencies in delta sleep over the course of the night in PTSD subjects may have important health consequences (Tasali et al., 2008, Scheen et al., 1996).

Analyses of delta sleep in PTSD raise a complementary question: is PTSD associated with an increase in power in the higher frequency bands, which may be indicators of brain hyperarousal during sleep? The reports that have examined this question have not indicated pronounced effects of PTSD on REM, NREM or overall beta power (Woodward et al., 2000, Germain et al., 2006, Cohen et al., 2012). These reports indicate that the neurophysiologic underpinnings of heightened subjective arousal during sleep in PTSD remains elusive, despite preliminary research examining this topic.

Existing findings, based on predominantly male samples, highlight that information on objective measures of sleep in female subjects with PTSD is severely lacking. In the study by Kobayashi and colleagues described previously, a comparison of weighted average effect sizes in male samples vs. mixed-sex samples demonstrated that PTSD-associated decrements in objective sleep quality were more pronounced in males than in females (Kobayashi et al., 2007). These findings are consistent with Neylan and colleagues findings regarding delta sleep: female subjects with PTSD demonstrated a numerically, but not statistically significant, decline in delta sleep as compared to control subjects (Otte et al., 2007). The delta sleep finding was significant in males only (Neylan et al., 2006). Because sleep is increasingly considered to be central to the pathophysiology of PTSD, and women are at greater risk of PTSD than males, even when controlling for trauma exposure, the examination of sleep in women with PTSD is essential.

Our current analyses take advantage of a 2×2 design (PTSD/control × female/male) including age- and sex-matched medically-healthy, unmedicated, young adults studied in a controlled laboratory environment to compare EEG measures of sleep across groups and between sexes. In this study, 3 nights of polysomnography with nocturnal blood sampling (night 1= adaptation, nights 2–3= pre and post metyrapone administration) were conducted at the University of California, San Francisco. This report focuses on the night 2 data during

which our subjects were medication-free. Our primary hypothesis, confirming prior research, was that PTSD is associated with greater visually scored slow wave sleep and cumulative NREM delta power (i.e: delta energy), and that this finding would be most pronounced in males. We also predicted that PTSD would be associated with more stage 1 sleep. Exploratory analyses examined overnight power in all frequency bands in both NREM and REM sleep, although based on recent findings we did not predict that PTSD would be associated with higher power in the higher frequency bands. Additionally, exploratory analyses of spectral power were performed to test for group (PTSD vs. control) by sex interactions.

Methods

The study sample was comprised of 40 individuals with current chronic PTSD (53% female; mean age 30.63, SD = 6.63) and 43 control subjects (49% female; mean age 30.39, SD = 8.15). This sample was drawn from a larger sample of 93 participants. Data from 10 participants were excluded due to poor quality sleep EEG recordings. Chronic PTSD was defined by fulfillment of DSM-IV criteria for chronic PTSD on the Clinician-Administered PTSD Scale (CAPS) and a CAPS score >40. Control subjects had no lifetime or current history of a PTSD diagnosis. The sleep of female subjects was measured during the follicular phase of the menstrual cycle. Exclusion criteria included history of traumatic brain injury, presence of neurologic disorders or systemic illness; use of psychiatric, anticonvulsant, antihypertensive, or sympathomimetic, steroidal, statin or other prescription medications; obesity (defined as BMI >30); alcohol abuse or dependence in the prior 2 years; substance abuse or dependence in the previous year; any psychiatric disorder with psychotic features; bipolar disorder or obsessive compulsive disorder; and pregnancy. Exclusion criteria for control subjects included a lifetime history of major depressive disorder or panic disorder. This research was approved by the Committee on Human Research at the University of California. All participants provided written informed consent before participating in any study procedures.

Measures

The CAPS was used to assess current and lifetime PTSD. The CAPS assesses the frequency and intensity of PTSD symptoms corresponding to the re-experiencing, avoidance and hyperarousal symptoms described in the DSM-IV diagnostic criteria (Blake et al., 1995). Diagnosis of PTSD was based on symptoms experienced in the previous month which were associated with the participant's self-identified worst traumatic event.

The SCID was used to diagnose all other psychiatric disorders, including major depressive disorder (MDD) (Spitzer et al., 1992).

Two self-report instruments, the PSQI and the PSQI-Addendum for PTSD were used to assess subjective sleep quality (Germain et al., 2005, Buysse et al., 1989). The PSQI-Addendum assesses the frequency of seven disruptive nocturnal behaviors. A score of 4 was shown to yield a sensitivity of 94%, specificity of 82%, and positive predictive value of 93% for discriminating those with PTSD from those without PTSD (Germain et al., 2005).

Polysomnographic Measurement

Polysomnography recordings were obtained with ambulatory polysomnography (Nihon Kohden Trackit Ambulatory Recording System). The parameters recorded included an electroencephalogram (EEG) at leads C3, C4, O1 and O2, left and right electrooculograms (EOG), submental electromyogram (EMG), bilateral anterior tibialis EMGs, and electrocardiogram (EKG) in accordance with standardized guidelines (Rechtschaffen, 1968).

Electrode impedance was set at < 5 kohm at the start of the recording. The EEG and EOG leads were referenced to linked mastoids. Raw EEG signals were filtered and amplified, then digitized at 256 Hz and recorded to a removable hard disk in European Data Format (EDF) file format. The low frequency and high frequency hardware filters on the recorder were single pole analog filters with 3 db points at 0.5 Hz and 100 Hz. Pass Plus was utilized for both visual scoring and quantitative EEG analysis of the digitized polysomnography data.

Visual Sleep Scoring

Visual scoring was conducted by one of the authors, a highly experienced registered polysomnography technician, who classified all 30-second epochs in every sleep record as wake; stages 1, 2, 3; REM; or movement using current AASM criteria. Sleep onset was defined as the first minute of eight consecutive minutes of stage 2 sleep with no more than 2 intervening minutes of stage 1 sleep or minutes awake. Total sleep time was defined by time spent in epochs scored as NREM stages 1 through 3 and stage REM. Wake after sleep onset (WASO) was defined as the time spent in epochs scored as wake between sleep onset and final awakening. An awakening was defined by EEG arousals lasting 15 seconds or longer. We were unable to report sleep latency because we did not acquire time of “lights out.”

Power Spectral Analysis

Pass Plus (Delta Software) analytic software was used to measure sleep activity in all frequency bands delta through gamma from the C3 electrode by power spectral analysis (PSA). The C4 electrode was used if there was excessive artifact. A limitation of Pass Plus is that artifact removal is accomplished by removal of whole epochs tagged with artifact. This has the potential to introduce additional confounds given the removal of typically longer bouts of uncontaminated EEG. Therefore, epochs were tagged for slow and fast artifact for additional analyses. Primary analyses were conducted with all epochs and then checked for the impact of removal of epochs with slow and fast artifact. Removal of fast artifact (for bandwidths alpha and above) and slow artifact (for bandwidths delta and theta) did not significantly impact our findings in NREM sleep. In REM sleep, artifact removal only altered our findings in one respect: a statistically significant group by sex interaction on REM delta energy emerged, driven by lower REM delta energy in PTSD+ males compared to control males with absence of such difference in females. Because of the small amount of delta activity in REM sleep and because the artifact-removal mechanism of Pass Plus removes entire epochs tagged with artifact, we were not surprised that removal of slow artifact had a statistically significant effect on delta findings in REM sleep and are concerned it yielded a spurious finding. All results are therefore reported without removal of epochs containing artifact. Pass Plus applied a 5μV smoothing constant to eliminate spurious waves caused by electrical jitter. PSA was conducted on all epochs of NREM and REM sleep. Epochs scored as wake were not included in these analyses. Pass Plus was used to perform Fast Fourier Transformation analysis on 4.0 second Welch tapered windows with 2 second overlap, yielding 15 windows per 30-second epoch. Power spectra for Delta (1–4 Hz) were analyzed to address our primary hypothesis with respect to delta sleep. Theta (4–8 Hz), Alpha (8–12 Hz), Sigma (12–15 Hz), beta1 (15–23 Hz), beta2 (23–30 Hz) and gamma (30–50 Hz) bands were analyzed for secondary analyses.

Statistical Analysis

Data screening procedures demonstrated that all visually scored sleep parameters, with the exception of WASO, were normally distributed. The WASO variable was natural-log-transformed for ANOVA. Distributions of quantitative EEG measures were all right-skewed. These variables were natural-log-transformed, resulting in a normalization of their distributions. Our primary hypotheses regarding SWS, stage 1 sleep and total delta energy (μV^2sec) were tested using an analysis of variance (ANOVA). Given the known associations

between major depressive disorder (MDD) and our primary outcome variable, delta energy, as well as recent findings from our lab indicating that 2 or more categories of childhood trauma accounted for the effects of PTSD on leukocyte telomere length, a marker of biological aging (O'Donovan et al.), we also examined the effects of MDD and childhood trauma history on delta energy.

Results

Demographic Data and Clinical Characteristics

The demographic and clinical characteristics of the sample are presented in Table 1. There were no significant differences in sex distribution between PTSD and control subjects, nor were there significant differences in age or education across all four groups. Male and Female PTSD subjects did not differ in terms of CAPS scores, rates of current major depressive disorder, or history of childhood trauma defined by the presence of 2 or more categories of childhood trauma as compared to 1 or none. Thirteen control subjects reported a lifetime history of a criterion A1 event, but all had current CAPS scores of zero and none had a lifetime history of PTSD. As per the exclusion criteria, no control subjects met criteria for current MDD. Additionally, none of the control subjects reported a history of 2 or more categories of childhood trauma.

Subjective Sleep Quality

There were significant differences in subjective sleep reports across groups (See Table 2). There was a main effect of group on total PSQI score, with both male and female PTSD subjects demonstrating significantly higher scores than control subjects. PTSD subjects also scored significantly higher than control subjects on the PSQI-Addendum. There was also a main effect for gender with women reporting more PTSD related sleep disturbance on the PSQI-A than their male counterparts.

Visually Scored Sleep Measures

Findings from the analysis of visually scored sleep EEG are presented in Table 2. Consistent with our hypothesis, PTSD subjects demonstrated significantly lower slow wave sleep (SWS) duration as compared to control subjects ($F(3,82)=7.63$, $p=.007$). Proportion of SWS to TST was also significantly smaller in PTSD subjects as a group as compared to controls ($F(3,82)=6.11$, $p=.016$). Pair-wise comparisons looking at males and females separately demonstrate that differences between PTSD subjects and controls were more pronounced in males than females. Contrary to expectations, there was no group effect for stage 1 sleep. There were also no significant main or interaction effects of group and sex on stage 2 sleep or WASO. Females displayed significantly greater total sleep time as compared to males, an effect that was primarily accounted for by a statistically significant difference in TST between PTSD females and PTSD males ($F(3,82)=11.02$, $p=.001$). Finally, our analyses revealed a statistically significant group by sex interaction effect on REM sleep, both in terms of absolute duration of REM sleep and percentage of REM sleep. This was explained by a difference in direction of difference between PTSD subjects and controls by sex: females with PTSD demonstrated statistically significantly greater REM sleep as compared to controls, whereas males with PTSD displayed non-statistically significantly lower REM sleep as compared to controls.

Power Spectral Analysis of EEG

Findings from quantitative analysis of sleep EEG are presented in Tables 3 (NREM sleep) and 4 (REM sleep). Values represent absolute spectral energy, which is cumulative spectral power in NREM and REM sleep, respectively, over the duration of the sleep period. As

hypothesized, there was a significant effect of PTSD on NREM delta activity (i.e.: delta energy) (See Table 3, $F(3,82)=6.79$, $p=.011$). There were no other significant main effects of PTSD on NREM energy in the higher frequency bands. We found main effects for sex on NREM energy in all frequency bands delta through beta1. When NREM sleep time was taken into account (i.e, when absolute power, as opposed to energy, was examined), gender effects disappeared and the main group effect for delta remained nearly significant ($p=.071$).

The Role of Depression and Childhood Trauma

There was no significant correlation between current major depression and history of childhood trauma (defined as 2 or more, versus 1 or no, categories of childhood trauma) and delta energy in bivariate analysis, therefore these variables were not included in further analyses. Post-hoc analyses examining delta and REM effects after removal of the 5 males and 3 females with current major depression resulted in a strengthening of the NREM delta effect ($F=7.80$; $p=.0067$) and a weakening of the group by gender interaction effect on REM duration ($F=1.90$; $p=.172$) and REM percent ($F=2.17$, $p=0.146$).

Relationship of objective sleep variables to CAPS total and subscale scores

Amongst PTSD subjects, there was no significant correlation between NREM delta energy and either total or subscale scores on the CAPS. Post-hoc bivariate correlations examining the relationship between REM sleep time and CAPS total and subscale scores revealed no significant correlations. Post-hoc correlations between REM sleep time and CAPS total and subscale scores within sexes were not statistically significant.

Discussion

These data provide additional evidence that PTSD is associated with a decrease in visually and quantitatively measured slow wave sleep. Quantitative sleep EEG research is providing strong evidence that delta sleep is essential for a variety of biological functions, including cognitive performance and glucose metabolism (Tasali et al., 2008, Scheen et al., 1996). Existing research also indicates that individuals with PTSD are at greater risk for multiple medical problems, such as cardiovascular disease, obesity, diabetes, and dementia which raises the possibility that disrupted delta sleep plays a mechanistic role in producing these negative health outcomes (Kobayashi et al., 2007, Boscarino, 2004, Yaffe et al.). These data also indicate, consistent with our lab's prior work, that this effect is more robust in men as compared to women. This raises unexamined questions about sex differences in the health and functional consequences of PTSD.

Contrary to our hypothesis, we did not identify group differences in stage 1 sleep, although, in males, we did find an increase in stage 2 sleep in PTSD subjects as compared to controls. All subjects in this study slept with IV catheters on all 3 nights of the overall study, which may have increased light sleep in all subjects. However, Stage 1 sleep was not elevated in the sample and there were no significant differences across groups in Stage 1 sleep, in sleep maintenance, or in number of awakenings across groups, all of which provide indirect evidence that sleep was not excessively disrupted by catheterization.

Consistent with recent findings, these data provide further support that current sleep EEG methods have not identified the neurophysiologic correlates of subjective hyperarousal in PTSD. Our data indicate no statistically significant group differences in all-night energy in the higher frequency bands, including beta bands, in either REM or NREM, although group differences in REM theta approached significance. Several alternatives may account for this finding. Prior research has demonstrated increased hyperarousal in PTSD in the context of trauma cues, but less consistently in their absence (Pitman et al., 1999, Orr et al., 2002). It

may be that PTSD subjects differ from controls only in the context of trauma reminders. Alternatively, current EEG approaches may be too coarse to effectively identify the neurophysiologic correlates of central arousal in PTSD. More refined approaches, including topographical approaches that take a finer look at regional brain activity, may be an important next step in identifying regional foci of brain arousal in sleep in PTSD (Marzano et al., 2008).

The identification of a group by sex interaction for REM sleep raises intriguing questions about the role of REM sleep in PTSD, and potential sex differences in that role. Prior studies were not designed to have a balanced sample of healthy age-matched men and women that would allow detection of group by sex interactions. Prior studies have not found differences in REM duration between PTSD and control subjects, although several studies have suggested that REM sleep disruption may be correlated with PTSD (Breslau et al., 2004, Mellman et al., 2007, Habukawa et al., 2007). The latter findings have led some researchers to speculate that REM sleep disruption in PTSD may reflect a disturbance in the processing of traumatic experiences (Mellman et al., 2007, Habukawa et al., 2007). On the other hand, increased REM sleep has also been shown to be correlated with greater consolidation of emotionally salient memories, the mechanisms and benefits of which, in PTSD and healthy subjects, remain unclear (Nishida et al., 2009, Baran et al.). Our findings indicate that sex differences should be considered in studies that examine REM sleep-dependent “processing” of emotionally salient events.

Adding complexity to this group by sex interaction on REM duration and REM percent, we found that removal of subjects with current MDD in post-hoc exploratory analyses reduced the effects to non-significance. This was in contrast to the effects on NREM delta energy, which were strengthened. Existing research suggests strongly that MDD is associated with decreased REM latency and increased REM density (Palagini et al., Pillai et al.) and some studies provide evidence for increased REM duration in MDD (Palagini et al.). However existing research does not demonstrate a group by sex interaction effect on REM duration in MDD such as was found in our study. There are therefore no a priori reasons to expect MDD, per se, to account for this reduction in effect. Given the high degree of symptom overlap between PTSD and MDD, and evidence that similar biological abnormalities, such as increased release of corticotropin releasing factor, may contribute to sleep disturbance in both disorders, it is possible that overlapping features of MDD and PTSD contribute highly to the group by sex interaction we found. It is also possible that the REM interaction effect is highly sensitive to loss of severe PTSD cases, as may have been the case in this sample, and our prior research indicates strongly that co-morbid MDD is more common as CAPS scores increase. In this sample specifically, mean CAPS score in MDD-negative subjects was 53.9 while mean CAPS score in MDD-positive subjects was 64.3 ($p=.099$). There is increasing evidence that sex differences need to be considered in neuroscience research (Cahill, 2006) and our findings highlight that further biological research on sex differences is crucial to better understanding the unique and shared relationships of traumatic stress and depressive symptoms to sleep disturbance and psychopathology.

Despite the many strengths inherent in this study’s design, several limitations have to be considered. As stated earlier, all participants were catheterized during sleep laboratory admissions. Another limitation of this study is that our findings are based on data from a single night of polysomnography recordings. Finally, generalization of our results to the overall PTSD population is limited by the nature of the sample, consisting of healthy, non-medicated subjects. However, we consider these sample features to be a considerable strength of this study because it enables us to gain information about sleep in men and women with PTSD without the potential confounding effects of medications and other factors potentially affecting sleep biology.

In conclusion, the current findings support prior evidence that PTSD is associated with impairment in the homeostatic function of sleep, especially in men with the disorder. Interaction effects of sex and PTSD status on REM sleep raise intriguing questions about the role of REM sleep in sexual dimorphism in PTSD pathophysiology. Replication of our findings with balanced samples of men and women are needed to understand the specific role of REM sleep in men and women with PTSD.

Acknowledgments

This project was supported by grants from the National Institute for Mental Health (TCN: 5R01MH073978-04, 5R34MH077667-03), the Mental Illness Research and Education Clinical Center of the US Veterans Health Administration, and the Clinical Research Center of the National Center for Advancing Translational Sciences, National Institutes of Health, through UCSF-CTSI Grant Number UL1 RR024131. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH. This material is the result of work supported with resources and the use of facilities at the Veterans Administration Medical Center, San Francisco, California. We are grateful to Ian Campbell, Ph.D. for his scientific input and to Maryann Lenoci for her logistical and technical support.

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Table 1

Demographic and Clinical Characteristics of the Sample

	Female (n=42)		Male (n=41)		
	Control n=21	**PTSD+ n=21**	**Control n=22**	**PTSD+ n=19**	**Contrast X^2 (1) =0.112 p= .74**
Age (M(SD))	30.57 (7.67)	30.10 (6.96)	30.23 (8.76)	31.21 (6.39)	F (3,82)= 0.09 p= .97
Education (yrs) (M(SD))	15.6 (2.03)	15.6 (1.68)	15.5 (2.08)	14.6 (2.40)	F (3, 80) =0.95 p=0.42
Race/Ethnicity					X^2(12)=17.56 p= .13
Caucasian (n)	16	13	17	11	
African American (n)	0	2	1	3	
Asian/Asian American (n)	3	2	4	0	
Other (n)	1	4	0	3	
Hispanic, Race unknown (n) *	1	0	0	2	
Clinical Characteristics					
CAPS (M(SD)) †	-	58.86 (17.32)	-	52.79 (13.81)	t(38)= −1.22 p= .23
Current MDD (N(%))‡	0	3 (14)	0	5 (26)	Fisher's exact p= .44
Childhood trauma (N(%))§	0	8 (42)	0	10 (50)	X^2 (1)=0.24 p= .62

* These 3 subjects endorsed Hispanic ethnicity but did not select a racial descriptor. Seven additional subjects endorsed Hispanic ethnicity, in addition to a racial category of Caucasian or African-American race yielding a total of 10 subjects self-identifying as Hispanic in this sample.

† Control subjects had CAPS scores of zero or had an absence of criterion A events. T-test compares mean CAPS score between male and female PTSD subjects only.

‡ Absence of current MDD was required for inclusion into the control group. Fisher's exact test compared MDD frequency between male and female PTSD subjects only.

§ Childhood trauma exposure was defined, based on findings from our prior research, by exposure to 2 or more categories of childhood trauma. Three (3) control subjects reported a history of 1 category of childhood trauma. Chi^2 test compared frequency of childhood trauma between male and female PTSD subjects only.

Table 2

Subjective Sleep Scores and Visually Scored Sleep Parameters by Sex and Group (PTSD+ vs. Controls)

	Female		Male		F-Test Group Effect	F-Test Sex Effect	F-Test Group × Sex Effect
	Control	PTSD+	Control	PTSD+			
	M (SD)	M (SD)	M (SD)	M (SD)	F (p-value)	F (p-value)	F (p-value)
PSQI	2.64 (1.45) †	11.01 (3.04) †	2.77 (1.72) ‡	10.26 (3.46) ‡	**203.80 (<.0001**	0.30 (.584)	0.63 (.431)
PSQI-Addendum	0.57 (0.81) †	7.57 (2.64) † §	0.32 (0.65) ‡	5.53 (3.41) ‡ §	**164.69 (<.0001)**	**5.84 (.018)**	3.55 (.063)
TST (min)	431.10 (53.03)	427.17 (60.54) §	403.66 (54.96)	374.61 (49.64) §	1.87 (.175)	**11.02 (.001)**	1.09 (.300)
Stage 1 (min)	16.57 (8.67)	17.30 (9.12)	14.18 (8.34)	15.52 (8.55)	0.31 (.581)	1.18 (.280)	0.03 (.869)
Stage 1 (%)	3.87 (2.07)	4.12 (2.21)	3.58 (2.23)	4.18 (2.36)	0.78 (.380)	0.06 (.810)	0.13 (.719)
Stage 2 (min)	258.88 (53.68)	254.42 (53.83)	236.80 (42.39)	238.21 (32.74)	3.47 (.066)	0.02 (.883)	0.08 (.776)
Stage 2 (%)	59.76 (7.63)	59.62 (9.88)	58.68 (7.16) ‡	63.99 (7.90) ‡	2.05 (.156)	0.83 (.364)	2.28 (.135)
SWS (min)	64.40 (29.17)	48.67 (33.76)	52.70 (25.02) ‡	33.08 (27.94) ‡	**7.63 (.007)**	**4.54 (.036)**	0.09 (.762)
SWS (%)	15.38 (7.27)	11.68 (8.34)	13.21 (6.41) ‡	8.91 (1.69) ‡	**6.11 (.016)**	2.33 (.131)	0.04 (.852)
REM (min)	91.24 (26.33)	106.76 (33.85)	99.98 (29.10)	87.76 (35.43)	0.06 (.810)	0.56 (.458)	**4.08 (.047)**
REM (%)	20.99 (4.73) † ¶	24.57 (5.97) †	24.53 (5.67) ¶	22.92 (6.38)	0.62 (.433)	0.57 (.454)	**4.30 (.041)**
WASO (min) **	55.81 (35.53)	65.81 (53.52)	54.02 (53.79)	71.26 (48.28)	1.66 (.202)	0.20 (.656)	0.83 (.364)
Sleep Maintenance	0.89 (0.01)	0.87 (0.02)	0.89 (0.02)	0.85 (0.02)	2.36 (.129)	0.23 (.634)	0.27 (.604)
Number of awakenings	12.86 (4.86)	15.29 (4.90)	12.41 (5.21)	13.89 (4.65)	3.27 (.074)	0.72 (.400)	0.19 (.664)

† T-test indicates a statistically significant difference between PTSD+ females and control females.

‡ T-test indicates statistically significant difference between PTSD+ males and control males.

§ T-test indicates statistically significant difference between PTSD+ females and PTSD+ males.

¶ T-test indicates statistically significant difference between control females and control males.

** ANOVA was performed on log-transformed WASO due to right-skewed distribution.

J Sleep Res. Author manuscript; available in PMC 2014 December 01.

Table 3

Quantitative EEG Sleep Measures by Sex and Group (PTSD+ vs. Controls): NREM Sleep*

	Female		Male		F-Test Group Effect	F-Test Sex Effect	F-Test Group × Sex Effect
	Control	PTSD+	Control	PTSD+			
	M (SD)	M (SD)	M (SD)	M (SD)	F (p-value)	F (p-value)	F (p-value)
Delta (1–4Hz)	38,948 (18,877)	31,049 (15,929)	30,198 (13,733)	22,799 (10,423)			
Log Delta		†	‡	†‡	**6.79 (.011)** §	**7.60 (0.007)** ¶	0.15 (.697)
Theta (4–8Hz)	7,839 (4,168)	6,833 (2,463)	5,822 (2,132)	5,427 (2,973)			
Log Theta		†		†	1.38 (.244)	**7.97 (.006)** ¶	0.11 (.740)
Alpha (8–12 Hz)	3,648 (1,699)	3,300 (1,531)	2,793 (1,226)	2,383 (1,183)			
Log Alpha		†		†	1.92 (.170)	**8.97 (.004)** ¶	0.15 (.701)
Sigma (12–15Hz)	1,894 (1,119)	2,069 (1,757)	1,799 (853)	1,254 (765)			
Log Sigma		†	‡	†‡	2.88 (.094)	**3.90 (.052)** ¶	3.04 (.085)
Beta1 (15–23 Hz)	911 (323)	947 (328)	815 (325)	797 (366)			
Log Beta1					0.01 (.920)	**4.63 (.035)** ¶	0.29 (.592)
Beta2 (23–30 Hz)	363 (121)	374 (132)	373 (240)	337 (169)			
Log Beta2					0.03 (.873)	1.25 (.267)	0.08 (.784)
Gamma (30–50 Hz)	574 (191)	552 (282)	633 (482)	548 (370)			
Log Gamma					0.45 (.504)	0.19 (.666)	0.14 (.712)

*Units of Energy (absolute spectral power over the duration of NREM sleep) are μV^2sec/100. Raw energy values must be multiplied by 100 to reflect actual energy and are presented as presented by Pass Plus software to enhance readability.

†T-test indicates statistically significant difference between PTSD+ females and PTSD+ males.

‡T-test indicates statistically significant difference between PTSD+ males and control males.

§Group effect for delta becomes a trend (p=.071) when NREM time is controlled for in regression analysis.

¶Gender effects disappear when NREM time is controlled for in regression analyses.

Table 4

Quantitative EEG Sleep Measures by Sex and Group (PTSD+ vs. Controls): REM Sleep*

	Female		Male		F-Test Group Effect	F-Test Sex Effect	F-Test Group × Sex Effect
	Control	PTSD+	Control	PTSD+			
	M (SD)	M (SD)	M (SD)	M (SD)	F (p-value)	F (p-value)	F (p-value)
Delta (1–4Hz)	2655 (1847)	3358 (2249)	5174 (11884)	2439 (2391)			
Log Delta					0.38 (.541)	0.56 (.456)	3.13 (.081)
Theta (4–8Hz)	1,208 (658)	1,149 (461)	1,981 (4,557)	805 (627)			
Log Theta		†	‡	†‡	2.75 (.101)	2.39 (.126)	2.80 (.098)
Alpha (8–12 Hz)	528 (321)	605 (321)	497 (267)	417 (300)			
Log Alpha		†		†	0.38 (.539)	2.15 (.147)	2.84 (.096)
Sigma (12–15Hz)	162 (79)	205 (107)	183 (92)	170 (155)			
Log Sigma					0.03 (.866)	0.09 (.767)	3.17 (.079)
Beta1 (15–23 Hz)	267 (150)	351 (184)	312 (187)	290 (230)			
Log Beta1					0.16 (.688)	0.00 (.997)	2.88 (.094)
Beta2 (23–30 Hz)	130 (86)	184 (136)	138 (97)	136 (110)			
Log Beta2					0.44 (.509)	0.16 (.693)	1.77 (.188)
Gamma (30–50 Hz)	189 (161)	260 (235)	213 (181)	170 (145)			
Log Gamma					0.06 (.814)	0.04 (.842)	1.91 (.171)

*Units of Energy (absolute spectral power over the duration of REM sleep) are μV^2sec/100. Raw energy values must be multiplied by 100 to reflect actual energy and are presented as presented by Pass Plus software to enhance readability.

†T-test indicates statistically significant difference between PTSD+ females and PTSD+ males.

‡T-test indicates statistically significant difference between PTSD+ males and control males.