Sleep and emotion processing in pediatric posttraumatic stress disorder: A preliminary investigation

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Sleep and emotion processing in pediatric posttraumatic stress disorder: A preliminary investigation

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**Introduction**

Approximately 5% of youth will develop pediatric posttraumatic stress disorder (pPTSD) by the age of 18, with prevalence estimates rising to 40% in cases of sexual or physical abuse (1). In addition to its acute cognitive and emotional impairments, pPTSD carries high risk for comorbid depression, anxiety disorders, and substance abuse across the lifespan (2-4). While early intervention has the potential to reduce enduring psychosocial dysfunction, current treatments for pPTSD are suboptimal, leaving a significant portion of youth unrecovered (5, 6). Novel, effective treatments are urgently required, but the development of such treatments requires a sophisticated understanding of both the basic mechanisms involved in the development and maintenance of PTSD and the factors that impact treatment response.

Both emotion processing abnormalities and sleep pathology are central to the phenomenology of PTSD across the lifespan. Up to 90% of those with PTSD report sleep disturbance, and sleep pathology is linked to the development, maintenance and severity of the disorder (7, 8). Although the precise way in which sleep disturbance contributes to PTSD symptomatology is not entirely clear, converging evidence suggests that sleep’s role in emotion processing may play a significant role. In addition to the well-documented effects of sleep loss on mood, experimental evidence in both adults and youth indicates that impaired sleep is associated with increased reactivity to negative stimuli, reduced emotion regulation, and poorer emotion discrimination (9, 10). When exposed to negative stimuli, sleep deprived subjects exhibit elevated amygdala reactivity and reduced functional connectivity between the amygdala and the medial prefrontal cortex (11), functional abnormalities that mirror the pattern commonly observed during emotion processing in PTSD (12-14).

Remarkably, despite the significant relationships between sleep and emotion processing, and the centrality of these domains to the pathophysiology of PTSD, these phenomena have yet to be directly assessed in youth. In this study, we use high-density (hd)EEG to compare a baseline night of sleep to a night of sleep following performance on a task designed to assess both memory for and reactivity to negative and neutral imagery in youth with diagnosis of PTSD and age- and sex-matched non-traumatized typically developing (TD) youth. Based on the theoretical (15) and empirical (11, 16,
17) literature linking REM sleep to affective homeostasis, we hypothesized that youth with PTSD would show heightened memory for and reactivity to negative content and that a failure of affective habituation from night to morning in PTSD youth would be associated with alterations in REM sleep.

**Methods**

**Participants**

The sample consisted of 10 age and sex-matched healthy non-traumatized typically developing (TD) youth and 10 youth with PTSD between the ages of 10 and 18 years. Youth were recruited as part of a longitudinal study on the neural correlates of PTSD (18, 19). Exclusion criteria for all participants included IQ<70 or unstable medical condition. Additional exclusion criteria for youth with PTSD included active suicidality, history of psychotic disorder, bipolar disorder, or OCD; recent (past 4 weeks) substance abuse or dependence; and recent use of psychotropic medication (past 4 weeks; 6 weeks for fluoxetine). TD subjects were free of any history of mental or neurological illness. Each participant and a caregiver reporter underwent a trauma and psychiatric screen with the Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) (20). A PTSD diagnosis was determined using DSM-IV criteria by combination of the KSADS and Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA) (21). The University of Wisconsin Health Sciences Institutional Review Board approved all procedures.

**Procedure**

The study consisted of two counterbalanced overnight sleep visits to the laboratory (baseline, task) separated by a 1-3 week interval. On the task night, all youth performed an emotional learning task immediately before sleep and again within one hour of natural wake time following an ad-libitum interval of sleep the next morning. A schematic and description of the emotional learning task, adapted from (22), is shown in Supplemental Figure 1. Stimuli were 248 pictures taken from the International Affective Picture System (IAPS) (23). Based on normative IAPS data and previous studies, pictures were separated into two valence categories: “Negative” and “Neutral.” During the pre-sleep portion of the task, participants viewed 140 target stimuli—70 negative and 70 neutral—in pseudorandom order.
Each trial began with the appearance of a fixation cross (500 ms) followed by the target picture (1500 ms). The Self-Assessment Manikin Scale for Arousal (SAM) (24) appeared after the target image and participants were asked to rate the degree of emotional arousal they experienced while processing the picture by choosing one of nine responses (ranging from 1=very low to 9=very high). Subjects were informed that they would be asked to recall images in the morning. In the post-sleep phase, youth viewed 200 images (100 negative and 100 neutral). This set included 92 of the previously viewed images (targets) intermixed with 108 novel images (foils). Participants again assessed arousal and indicated whether they recognized the picture from the previous encoding session (“old”) or not (“new”).

Sleep recordings
On the baseline night, subjects’ sleep was evaluated with standard polysomnographic equipment for the diagnosis of sleep disorders along with hdEEG (256 channels). On the task night, hdEEG (Electrical Geodesics Inc.) was recorded along with EMG and EOG. Sleep was scored by a registered sleep technologist according to AASM guidelines (25, 26), and reviewed by a board certified sleep physician. HDEEG processing methods were identical to those described in Jones 2014(27).

Statistics
All statistical analyses were performed using MATLAB.

Behavioral data
To assess affective habituation, our dependent variable was the average change in subjective arousal rating to target images (ΔArousal=subjective arousal rating during the post-sleep recognition phase minus arousal rating during the pre-sleep encoding phase). A negative score indicates images were rated as less arousing in the post-sleep compared to pre-sleep phase. ΔArousal was assessed with a mixed effects linear model including a group by valence interaction term covarying for age and sex with random error terms for subject and picture ID. For memory, recognition accuracy was calculated using ‘hit rate’ (the number of times a subject correctly identified a target image as having been seen before; e.g., correctly responded “old”), as well as ‘false alarms’ (the number of times a subject incorrectly
identified a foil as having been seen before; e.g. incorrectly said “old”). Mixed effects linear models considered hit rate and false alarm separately as functions of valence and group with error terms for subject and picture ID. Independent linear models were also calculated to examine the relationship between symptom severity using the Screen for Child and Anxiety Related Emotional Disorders (SCARED), the Mood and Feelings Questionnaire (MFQ) and PTSD-Reaction Index (PTSD-RI) (for PTSD youth only) and (1) EEG oscillatory activity and (2) change in emotional arousal.

Sleep

All sleep macrostructure variables were analyzed using a two-way mixed analysis of variance (ANOVA) design with the between-subjects variable group (PTSD vs TD) and the within-subjects variable night (task vs baseline). Differences in all-night EEG power spectral data for both NREM and REM sleep were first assessed using 2-way mixed effects ANOVA with factors Group by Night. However, this study was designed to assess within-group changes in sleep microstructure between a baseline night of sleep and a night where a task was performed, so changes in absolute spectral power density (μV²) and topographic (regional) differences in EEG power on the baseline versus the task night in both NREM and REM were considered separately for each group using paired t-tests. Analyses of topographic power were initially assessed using electrode-to-electrode unpaired t-tests. As a more rigorous assessment of significance, absolute topographical power maps in NREM and REM sleep were then subjected to statistical nonparametric mapping (SNPM), using a supra-threshold cluster test (t-value threshold =2) of all possible combinations (n = 1024) to identify significant clusters of electrodes (28). After choosing an appropriate threshold t-value (for consistency a t-value threshold = 2 was chosen for all frequency ranges), topographic power maps were randomly shuffled for each group between nights (baseline versus task) in all possible combinations. The size of the largest contiguous cluster above the threshold for each reshuffling was then used to create a maximal cluster size distribution. The suprathreshold cluster p value was then determined by comparison of the actual cluster size (the cluster above threshold for the real subject grouping) against the maximal cluster size distribution.
Sleep and behavior correlations

To assess the relationships between sleep and affective habituation and sleep and memory we correlated ΔArousal and hit rate with within-subject percentage change in power density between nights \([\Delta\text{power} = (\text{task} – \text{baseline}) \times 200 / (\text{task} + \text{baseline})]\) for all frequency bands. Power and Δpower for each electrode were correlated with both ΔArousal and hit rate using Pearson’s correlation coefficient and displayed on topographic maps. To control for multiple comparisons, significant correlations were determined again using a SNPM cluster test\((\text{cluster threshold of } r = 0.47, \text{ with } 50,000 \text{ permutations})\)(29). We also did a post-hoc confirmatory analysis of the significant cluster by averaging Δpower across the electrodes included in the cluster and ΔArousal using a non-parametric Spearman rank correlation. Additionally, correlations of hit rate with sleep-stage percentages (REM%, N2%, N3%), spectral power in REM theta, NREM SWA, and NREM spindle power during the task night were performed. Although we attempted to correct for the problem of multiple comparisons where necessary (e.g. across topographical images), it should also be noted that we did not strictly correct for the issue of multiple testing given the small sample size and exploratory nature of this study.

Results

Participant characteristics are summarized in Table 1. The groups did not significantly differ in sex distribution, age, pubertal stage or handedness. IQ was lower in PTSD youth (mean±SD, PTSD 100.50 (±3.42); TD, 113.30 (±3.49); \(p=0.017\)). As such, IQ was included in models. Within the PTSD group, the most common index trauma was sexual abuse, followed by witnessing violence and traumatic death of a loved one. PTSD symptoms averaged 44.7 based on the PTSD-RI, which is indicative of severe PTSD.

Overnight change in arousal shows distinct pattern in PTSD and TD youth

Although the distribution of arousal rating seem to differ between groups, (see supplemental figure 2), on average, subjective arousal scores during pre-sleep encoding were similar for both groups (mean±SD, TD negative 5.84±2.27, neutral 2.49±1.91; PTSD negative 5.42±3.19, neutral 1.89±1.66) as were the post-sleep arousal scores (mean±SD, TD negative 4.72±2.26, neutral 1.77±1.19; PTSD
negative 4.79±3.17, neutral 1.60±1.42). The average change in arousal scores showed a significant
group by valence interaction ($\chi^2=9.4364, p=.002127$). As shown in Figure 1A, the TD group significantly
decreased average arousal to negative images (mean decrease -1.0, 95% CI -1.44 to -0.58) and to
neutral images (mean decrease -0.74, CI -1.17 to -0.32), indicating that habituation had occurred. In
contrast, responses in PTSD youth to negative images remained effectively unchanged (mean increase
0.15, CI -.28 to +0.58). Responses in PTSD youth to neutral images also remained effectively
unchanged, with a less pronounced decrease than observed in the TD group (mean decrease -0.14 CI
-0.57 to 0.29).

**Memory recall does not differ in PTSD and TD youth**
As shown in Figure 1B, mean values of hit rate (Negative images PTSD=0.83±0.10, TD=0.79±0.09;
Neutral images PTSD=0.79±0.15, TD=0.81±0.07) did not differ significantly by group ($\chi^2=.0391,
p=.8432$) or by valence ($\chi^2=.2036, p=.6518$). Similarly, mean values of false alarm (Negative images
PTSD=0.2107±0.28; TD=0.09±0.08; Neutral images PTSD=0.21±0.23; TD=0.13±0.09) did not differ
significantly by group ($\chi^2=1.4767, p=.2243$) or by valence ($\chi^2=1.5823, p=.2084$) and there was no group
by valence interaction ($\chi^2=1.371, p=.2416$) (Figure 1C).

**Sleep Macrostructure**
Two-way mixed ANOVAs revealed no significant main effects of group or night and no significant group
by night interaction for any sleep variable (total sleep time, sleep efficiency, latency to SWS and REM
sleep, and duration of all sleep stages) ($F(1/18) < 4.1, p > 0.05$). Macrostructural variables for
both the task and baseline recordings are summarized in Table 2. Of note, WASO (wake after sleep
onset) was lower in TD youth on the task night relative to the baseline night, suggesting that TD youth
had more consolidated sleep following the presentation of images on the task night. In contrast PTSD
youth had more WASO on the task night relative to their baseline night, suggesting disrupted sleep.

**Sleep Microstructure**
Changes in REM sleep from baseline to task night:
As shown in Figure 2A, both groups showed evidence of changes in high-frequency power during REM
sleep, albeit in opposite directions. In PTSD youth, a significant increase in high-frequency (22.5-27Hz, 29.6-33Hz, 33-37Hz, \(p=0.048, 0.009, 0.036\)) was observed during the sleep following task performance relative to baseline sleep (Figure 2A). In contrast, in TD youth, a small increase in the gamma range (27.8-29.6Hz, \(p<0.039\)) was observed on the baseline night relative to the task night (Figure 2A).

Despite the global increases in high-frequency activity, no consistent topographic changes in EEG power emerged in either group. There were no group differences in REM all-night global spectral data.

Changes in NREM sleep from baseline to task night:

Both groups showed the classical pattern of all-night NREM spectral activity (2B), with greatest power in the slow wave frequency band (1–4.5 Hz) and a second peak in the sigma band (12–15 Hz). As shown in Figure 2B when averaged across channels, PTSD youth showed a significant increase in high-frequency activity in the beta/gamma range (19-39Hz, \(p<0.003\) Hz) on the task night relative to the baseline night as well as a significant decrease in the slow-wave activity range (0.5-2.5Hz, \(p<0.026\)). In TD youth, a broad band decrease in high-frequency beta/gamma (16-36Hz, \(p<0.002\)) was observed on the task night relative to the baseline night (2B). There were no group differences in slow-wave activity or high-frequency activity in the all-night spectral data.

Topographical changes in NREM SWA and Gamma in PTSD youth

As shown in Figure 2C, in PTSD youth, a large cluster of electrodes (N = 110, \(p = 0.036\)) was reduced in the SWA band during NREM sleep on the task night relative to the baseline night, consistent with the observed global change in low frequency spectral power. In addition to the marked decrease in SWA, a cluster of right-lateralized posterior electrodes (N =20, \(p=.011\)) were significantly increased in the gamma band during NREM on the task night in PTSD youth (Figure 2D). In TD youth, no significant regional differences were observed in any frequency band (Figure 2A and 2B, EEG Topography).

Correlation of sleep macro and microstructure with affective habituation

Despite the robust differences between PTSD and TD youth in gamma power changes between the task and baseline nights, we identified no relationship between NREM or REM gamma changes with \(\Delta\)Arousal. However, we did find a negative correlation between average \(\Delta\)Arousal and global changes...
in SWA power ($\rho=-0.58$, $p=0.008$). A topographic investigation identified a significant negative correlation between $\Delta$SWA power in a frontal cluster of electrodes (27 channels, $p=0.045$) and $\Delta$Arousal, such that as SWA power decreased (% decrease on task night relative to baseline night) emotional arousal failed to normalize (failed to change from a high to a low value) as shown on the left of Figure 3. When $\Delta$SWA power was averaged across electrodes in the significant cluster, a Spearman correlation confirmed a robust relationship with $\Delta$Arousal ($\rho=-0.51$, $p=0.021$), as shown in the scatterplot on the right of Figure 3. Data are shown are for negative images that were correctly remembered, but the results were similar when considering all negative images.

**Correlations with symptom severity**

There were no significant relationships between SWA, NREM or REM Gamma power when considering SCARED/MFQ outcomes in the entire sample, and no relationships between EEG oscillatory activity and PTSD symptoms. In separate linear models, SCARED and MFQ predicted change in arousal ($p=0.0301$ and $p=0.0049$, respectively) such that higher scores were inversely associated with arousal reduction from night to morning.

**Discussion**

To our knowledge, this study represents the first report of sleep EEG assessment in pediatric PTSD. There are several notable findings. First, relative to a pre-sleep baseline, youth with PTSD show enhanced arousal to negative imagery after sleep compared to TD youth yet have similar factual recall for these images. Second, this post-sleep impairment in affective habituation was unrelated to macrostructural sleep patterns in youth with PTSD, who showed similar sleep macrostructure to typically developing youth. Third, impairments in post-sleep affective habituation were not associated with any feature of REM sleep but were correlated with reductions in slow-wave activity particularly over frontal regions. Together, these findings point to novel cortical sleep mechanisms which may underlie enhanced reactivity to threat and potentially threat-extinction impairments in pediatric PTSD.

Robust differences between PTSD and TD youth were evident when considering the change in sleep following task performance relative to a baseline night of sleep. In PTSD youth, sleep depth and
quality was markedly impaired following task performance as indexed by a significant *global* decrease in SWA and a significant increase in high-frequency beta/gamma activity suggestive of cortical arousal (30). It is reasonable to speculate that the viewing of the IAPS images before sleep was ultimately responsible for the decrease in sleep quality and sleep depth following task performance in PTSD youth. Indeed, emotional distress before sleep has deleterious effects on subjective as well as objective sleep quality, including reductions in SWS, lower sleep efficiency, and elevated arousals from sleep (31-33). Notably, however, when considering the subjective rating of arousal during the pre-sleep encoding period, there was no evidence that the images were any more distressing to PTSD compared to TD youth.

In the morning after a period of sleep, TD youth robustly reduced subjective arousal to images in both valence categories such that an image viewed as arousing during the pre-sleep encoding was rated as significantly less arousing after sleep. In contrast, PTSD youth did not reduce subjective arousal ratings to either valence category, even showing a non-significant increase in arousal to negative images post-sleep. Given that a global change in SWA was correlated with affective habituation, one possible interpretation of this relationship is that in PTSD youth, the images proved disruptive to sleep, and this reduction in sleep depth and quality then exacerbated next day emotional reactivity. Indeed, both naturalistic and experimental evidence indicates that inadequate sleep in both adults and youth is associated with increased negative affect, amplified responsivity to aversive stimuli, and diminished emotion regulation capacity and mood disturbance (10, 34-36). In addition to these behavioral effects, the functional integrity of the networks sub serving emotion are also impaired following sleep loss or restriction. One night of sleep restriction leads to a 60% amplification of amygdala activation in response to negative emotional stimuli relative to a rested condition, along with a concomitant decrease in medial-prefrontal cortical activity, a region known to exert top-down control of the amygdala (11, 15). Importantly, however, the regulation of emotional reactivity observed in this study appears to be specifically related to SWA and not to a general impairment in sleep quality and/or elevated arousal. For example, gamma power during sleep, generally considered an index of a more
‘wakeful’ sleep and an index of elevated central adrenergic activity (37), was robustly elevated in PTSD youth on the task night relative to the baseline night, and reduced in TD youth. However, neither the change in gamma power in NREM from baseline to task, nor REM gamma on the task night was related to the change in emotional reactivity.

When considering the correlation between SWA and affective habituation, the relationship was strongest in a cluster of electrodes over the frontal cortex. In light of this regional relationship, we speculate that impaired affective habituation and the regional decrease in SWA in PTSD youth is related to reduced engagement of prefrontal cortical regions during stimulus encoding. This, in turn, may result in a reduced need for SWA and its associated plasticity functions during the subsequent sleep period. Slow wave activity is broadly associated with synaptic remodeling and cortical plasticity (38). SWA increases or decreases in cortical regions that are more or less active respectively during previous waking in animals (39) as well as in humans (40). Functional MRI studies of adults with PTSD consistently demonstrate hyperactivity of the amygdala, important for threat reactivity and encoding, yet decreased engagement of prefrontal regions implicated in cognitive-emotional control during emotion processing (41). Our group and others have found similar evidence in pediatric PTSD, including reduced coupling between the amygdala and medial prefrontal cortex (mPFC) during viewing of threat imagery (14, 18, 19).

Given the theoretical and, to a lesser extent, experimental work supporting a role for REM sleep in emotional brain function (15), and the prevailing view that REM sleep is prominently disrupted in PTSD (42), the lack of correlation with REM power, yet robust correlation between SWA power and affective habituation, was unexpected. However, although REM sleep’s role in emotional memory has been widely explored, the specific role sleep plays in subjective reactivity to emotional stimuli has received less attention, and the existing data do not support an exclusive role for REM in reducing emotional reactivity. Indeed, REM sleep may reinforce reactivity to emotionally salient stimuli rather than support adaptive reappraisal (43-45). Moreover, a number of studies support a role for slow-wave sleep in the adaptive affective reappraisal of complex stimuli (46-48). In clinical samples, reduced SWS
following written narrative exposure therapy for PTSD was associated with diminished therapeutic

efficacy, (48) while increased SWS predicted success of exposure psychotherapy for simple phobia

(47).

With respect to memory, we did not detect a performance difference between PTSD relative to

TD youth for either valence type. At first glance, this lack of an emotional memory advantage in PTSD

seems surprising in light of work showing that individuals with PTSD have a tendency to encode

negative or neutral stimuli as subjectively more aversive (49-51). However, although some data

supports an emotional memory advantage in PTSD relative to comparison groups, a number of studies

report no memory differences despite underlying differences in neural activation during encoding (50-

52). We did not find a relationship between any feature of sleep macro or microstructure (%time in

NREM, REM duration, SWA power, spindle power, REM theta power) and recognition memory for

stimuli in either valence category. Despite some evidence in adults that specific features of NREM and

REM may aid declarative and emotional memory, respectively (53), data in youth is both scant and

discrepant (22, 54-59). Our findings, albeit preliminary, suggest that sleep function may play a

preferential role in affective reappraisal, but not factual encoding, for emotional imagery.

Limitations

A central strength of this study includes the use of an emotional learning task combined with sleep

hdEEG, which allows for a regional analysis of neural activity not possible with traditional

polysomnography studies. Our analyses were conducted in an unmedicated, otherwise healthy

population of PTSD and TD youth, suggesting that results are not confounded by factors related to

medication or sleep and/or medical disorders. However, the sample size used in these analyses was

modest, which increases the risk of false-positives and may overestimate the magnitude of effects. We

attempted to mitigate this issue by using a within-subjects design to assess sleep and the use of non-

parametric statistical methods, which make few assumptions about the distribution of the data and are

more robust to outliers. Additionally, the study was not sufficiently powered to explore group by session

interactions, so we cannot determine if changes in one group were significantly different from the other.
As such, the results of this study, while novel and of potential clinical import, should be considered preliminary and replicated in larger samples of youth. Finally, our study did not include a trauma-exposed comparison group without PTSD, which will be important in future work to assess specificity of findings to PTSD versus trauma exposure per se.

**Conclusion**

The relationship between sleep SWA and affective dysregulation in youth with PTSD highlights the importance of slow-wave sleep for adaptive emotional processing and has potentially broad-ranging implications for understanding the persistence of symptoms in PTSD. Viewed more directly, these data also have potential relevance for the success and/or timing of therapeutic interventions. For example, in-vivo exposure therapy requires a child to face a feared stimulus for a sustained period while experiencing heightened feelings of arousal. Habituation to a feared stimulus, the goal of exposure therapy, may be less likely to occur if the underlying cortical sleep mechanisms are not acting to downscale the affective content of memory. Given significant inter-relationships between sleep, PTSD and emotion processing and their respective and combined contributions to functional impairment, a deeper understanding of how one impacts the other has the potential to inform the development of novel sleep-focused therapies for the treatment of PTSD in youth. Indeed, if these data are replicated in a larger sample, slow-wave enhancement may represent a promising interventional tool.

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References


**FIGURE LEGENDS:**
Supplemental Figure 1: Emotional Image Task

Stimuli were 248 pictures taken from the International Affective Picture System supplemented with a picture set provided by which had images categorically similar to the IAPS set. Based on normative IAPS data and previous studies, pictures were separated into two valence categories: “Negative” images were negatively valenced and selected for moderate to high arousal and “neutral” images for low standardized arousal ratings. During pre-sleep encoding, participants viewed 140 target stimuli – either 70 negative and 70 neutral– in pseudorandom order. The Self Assessment Manikin Scale for Arousal (SAM) appeared after the target image and participants were asked to rate degree of emotional arousal experienced while processing the picture by pressing one of nine response buttons (ranging from 1=very low to 9=very high). Following an ad libitum nocturnal sleep interval, participants completed a recognition phase that include 200 images (100 negative and 100 neutral). This set included 92 of the previously viewed images (targets) intermixed with 108 novel images (foils). Participants again assessed arousal and indicated whether they recognized the picture from the previous encoding session (“old”) or not (“new”) by pressing one of two response buttons.

Table 1: Sample Characteristics

The sample consisted of 10 healthy non-traumatized youth and 10 youth with PTSD between the ages of 10 and 18 years. PTSD and TD youth were age-matched within ±3 months. Abbreviations: CAPS–CA, Clinician-Administered PTSD Scale for Children and Adolescents; MFQ, Mood and Feelings Questionnaire; SCARED, Screen for Child Anxiety-Related Emotional Disorders. The healthy and PTSD groups did not significantly differ in sex distribution, age, Tanner stage, or handedness. Numbers in parentheses with ‘±’ represent SEM

Supplemental Figure 2: Frequency graphs of raw subjective arousal ratings for emotional images highlights marked differences in response patterns in PTSD and TD youth.

Subjective arousal responses to emotional and neutral images in the pre-sleep period and post-sleep period are shown in Figure 1. Emotional images on left and neutral on right. TD subjects shown in grey (upper panel) and PTSD youth shown in red (lower panel). Arousal ratings 1-9 are shown on the x-axis, and the number of times the rating was given to an emotional picture by subjects (in the group and at the time point in question) is shown on the y-axis. Each of 10 subjects per group viewed 70 emotional pictures at night and 100 emotional pictures in the morning, for a total of 700 ratings at night and 1000 in the morning.
Figure 1: Overnight change in affective habituation, but not memory, distinguishes PTSD and TD youth. Hit rate (percent of old pictures correctly labeled as “old”) and false alarms (percent of new pictures incorrectly labeled as “old”) shown as a function of valence (emotional and neutral) in TD (grey) and PTSD (red) youth. 1A). Mean values of hit rate for emotional (left) and neutral (right) images did not differ significantly by group (chisq = .0391, p = .8432) or by valence (chisq = .2036, p = .6518) and there was no significant groups by valence interaction (chisq = 3.2367, p = .07201). 1B) Mean values of false alarm as a function of valence did not differ significantly by group (chisq = 1.4767, p = .2243) or by valence (chisq = 1.5823, p = .2084) and there was no group by valence interaction (chisq = 1.371, p = .2416). (Error bars represent 95% confidence interval). 1C) Mean overnight change in subjective arousal ratings highlight distinct response patterns in PTSD and TD youth. ΔArousal (morning-evening) shown as a function of group (TD and PTSD) and valence category (Emotional and Neutral). A negative score indicates images were rated as less arousing in the post-sleep phase. As shown on right side of figure 1C, TD group (shown in gray) significantly decreased average arousal to emotional images (mean decrease -1.0, 95% CI -1.44 to -0.58;). In contrast, responses in PTSD youth to emotional images remained effectively unchanged (mean increase 0.15, 95% CI -.28 to +0.58) suggesting that, after a period of sleep, PTSD youth did not habituate to the emotional content of the imagery. TD youth also significantly decreased responses to neutral images (mean decrease -0.74, CI -1.17 to -0.32). PTSD youth decreased arousal ratings to neutral images, this was less pronounced than the decrease observed in the TD group (mean decrease -0.14 CI -0.57 to 0.29). (error bars represent 95% confidence interval).

Table 2: Macrostructural sleep variables. Mean values (+/- standard error of the mean, n = 10 per group). Percentage values for sleep stages are expressed per total sleep time (TST). AHI, apnea-hypopnea index; AI, arousal index; SE, sleep efficiency (TST per time in bed); REML, rapid eye movement onset latency;; WASO, wake after sleep onset.

Figure 2: Analysis of sleep microstructure reveals distinct patterns of sleep in TD and PTSD youth after task performance

Figure 2 A and B: Spectral analysis of all-night EEG power during REM and NREM sleep on the task night versus the baseline night in PTSD and TD youth. Figure 2A highlights opposite changes in high-frequency power during REM sleep in both groups. In PTSD youth, a significant increase in high frequency activity is evident during REM following task performance relative to baseline sleep, while in TD youth, a small decrease in the gamma range is evident. 2B highlights a similar pattern of high-frequency increase in PTSD and decrease in TD youth during NREM sleep on the task night.
relative to the baseline night. In PTSD youth, a decrease in slow frequency activity is also evident on the task night. In contrast, in TD youth increased high frequency activity is present on the baseline night relative to the task night, suggesting more consolidated sleep after task performance. Spectral density plots for the global average across all electrodes in NREM (2A) and REM (2B) sleep for PTSD (left) and TD (right) youth. Uncorrected p-values for the comparison between task night (black) and baseline night (red) are shown below each plot, respectively.

Figure 2C and D) Topographical analysis of NREM sleep EEG in PTSD youth reveals a broadly distributed decrease in SWA on the task night relative to the baseline night as well as a regional increase in Gamma EEG power.

Figure 2C Top: Average NREM sleep EEG topographies in SWA (1-4.5Hz) for PTSD and TD youth on baseline (PSG) night. Middle: Average NREM SWA for PTSD and TD youth on task night. Lower: Topographic distribution of the change in SWA during non-REM sleep between the baseline and the task night. Blue values represent a decrease on EEG power on the task night relative to the baseline night. White dots indicate the cluster of 27 electrodes showing decreased SWA on the task night ($P < 0.01$, statistical nonparametric mapping, supra-threshold cluster test controlling for multiple comparisons). Figure 2D Top: Topographical averages for NREM gamma (25-40Hz) for PTSD and TD youth on baseline. Middle: Topographical averages of each group for gamma on task night. Lower: Topographic distribution of the change in gamma power during non-REM sleep between the baseline and the task night. Red values represent an increase in EEG power on the task night relative to the baseline night. White dots indicate the cluster of 20 electrodes showing an increase in power on the task night ($P < 0.01$)

Figure 3: Topography of the correlation of change in emotional reactivity and slow-wave activity

Figure 3: A decrease in SWA is associated with a failure of affective habituation (Left) A frontal cluster of channels in the SWA band (white dots) is significantly correlated (SNPM cluster threshold of $r = -.47$, N=21) with affective arousal such that as SWA decreased on the task night relative to the baseline night (negative % change values), affective habituation did not occur (failed to change from a high to a low value) ($ρ = -0.51$, $P = 0.021$). Right: A scatter plot showing correlation coefficient of correlation ($r$) between arousal and SWA power ($\mu V^2$) in significant cluster (white dots indicate cluster of 27 electrodes showing decreased SWA on the task night ($P < 0.01$, statistical nonparametric mapping, supra-threshold cluster test controlling for multiple comparisons). Red dots (PTSD) and grey dots (TD)
represents an individual subject’s % SWA change and the average overnight change in affective habituation.
Supplemental Figure 1: Emotional learning task showing (left) encoding and (right) recognition trials.
Table 1: TD and PTSD youth demographics:

Abbreviations: CAPS–CA, Clinician-Administered PTSD Scale for Children and Adolescents; MFQ, Mood and Feelings Questionnaire; SCARED, Screen for Child Anxiety-Related Emotional Disorders. The healthy and PTSD groups did not significantly differ in sex distribution, age, Tanner stage, or handedness. Numbers in parentheses with ‘±’ represent SEM.

<table>
<thead>
<tr>
<th></th>
<th>Typically Developing</th>
<th>PTSD</th>
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<tbody>
<tr>
<td>N</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Age (years)</td>
<td>14.67 ±0.94 range: 10.00-17.92</td>
<td>14.52 ±0.95 range: 10.00-17.54</td>
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<td>Tanner stage</td>
<td>3.10 ±0.39 range: 1-5</td>
<td>3.23 ±0.46 range: 1-5</td>
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<tr>
<td>IQ</td>
<td>113.30 ±3.49 range: 97-139</td>
<td>100.50 ±3.42 range: 89-121</td>
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<tr>
<td>Left-handed (n)</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Index trauma (n)</td>
<td>--</td>
<td>Sexual abuse (3), witnessing violence (3), traumatic death of loved one (2), accident (2), physical abuse (1)</td>
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<tr>
<td>Comorbid diagnoses (n)</td>
<td>--</td>
<td>Major depressive disorder (4), ADHD (4), generalized anxiety disorder (3), separation anxiety disorder (2), social anxiety disorder (1), conduct disorder (1), social phobia (1)</td>
</tr>
<tr>
<td>PTSD duration (months)</td>
<td>--</td>
<td>36.70 (±7.72)</td>
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<td>PTSD reaction index</td>
<td>--</td>
<td>44.70 (±6.04)</td>
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<tr>
<td>CAPS-CA</td>
<td>--</td>
<td>60.45 (±8.00)</td>
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<tr>
<td>MFQ</td>
<td>4.40 (±0.79)</td>
<td>21.75 (±3.13)</td>
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<tr>
<td>SCARED</td>
<td>7.65 (±1.65)</td>
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<tr>
<td>Past psychiatric medication</td>
<td>--</td>
<td>Stimulant (3), antidepressant (3), benzodiazepine (1)</td>
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**Supplemental Figure 2:** Frequency graphs of raw subjective arousal ratings for emotional images highlights marked differences in response patterns in PTSD and TD youth.

Typically Developing ■
PTSD ■
**Figure 1:** Overnight change in affective habituation, but not memory, distinguishes PTSD and TD youth.
Table 2: Macrostructural sleep variables.

<table>
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<tr>
<th>Measure</th>
<th>Group</th>
<th>PSG Night</th>
<th>Task Night</th>
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<tr>
<td>AHI</td>
<td>PTSD</td>
<td>2.03(.74)</td>
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<td>TD</td>
<td>2.93(.55)</td>
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<tr>
<td>TST</td>
<td>PTSD</td>
<td>436.49(33.92)</td>
<td>425.61(38.52)</td>
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<td></td>
<td>TD</td>
<td>452.42(19.59)</td>
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<tr>
<td>WASO</td>
<td>PTSD</td>
<td>64.35(14.17)</td>
<td>75.20(17.19)</td>
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<td></td>
<td>TD</td>
<td>45.50(4.76)</td>
<td>36.10(4.38)</td>
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<tr>
<td>AI</td>
<td>PTSD</td>
<td>11.00(1.03)</td>
<td>11.01(1.10)</td>
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<tr>
<td></td>
<td>TD</td>
<td>10.95(.89)</td>
<td>11.35(1.42)</td>
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<tr>
<td>SE</td>
<td>PTSD</td>
<td>90.84(1.81)</td>
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<td></td>
<td>TD</td>
<td>93.19(.71)</td>
<td>94.44(.63)</td>
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<td>N1%</td>
<td>PTSD</td>
<td>3.64(.87)</td>
<td>4.00(64)</td>
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<tr>
<td></td>
<td>TD</td>
<td>4.05(.87)</td>
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<td>N2%</td>
<td>PTSD</td>
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<td>47.47(2.32)</td>
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<td></td>
<td>TD</td>
<td>57.09(1.60)</td>
<td>58.23(1.98)</td>
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<tr>
<td>N3%</td>
<td>PTSD</td>
<td>22.95(2.12)</td>
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<td></td>
<td>TD</td>
<td>21.93(2.25)</td>
<td>20.44(1.92)</td>
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<tr>
<td>REM%</td>
<td>PTSD</td>
<td>18.81(1.93)</td>
<td>17.72(2.17)</td>
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<tr>
<td></td>
<td>TD</td>
<td>16.96(1.61)</td>
<td>18.59(1.83)</td>
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<tr>
<td>REML</td>
<td>PTSD</td>
<td>159.85(18.10)</td>
<td>164.65(32.73)</td>
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<tr>
<td></td>
<td>TD</td>
<td>141.15(21.60)</td>
<td>135.30(14.55)</td>
</tr>
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</table>

Table 2: Macrostructural sleep variables. Mean values (+/- standard error of the mean, n = 10 per group). Percentage values for sleep stages are expressed per total sleep time (TST). AHI, apnea-hypopnea index; AI, arousal index; SE, sleep efficiency (TST per time in bed); REML, rapid eye movement onset latency; WASO, wake after sleep onset.
Figure 2: Analysis of sleep microstructure reveals distinct patterns of sleep in TD and PTSD youth after task performance.
Figure 3: A decrease in SWA is associated with a failure to habituation to affective stimuli in PTSD youth.