



# The dream of trauma-related nightmares: Can physiological and subjective within- subjects measures help elucidate sleep-related mechanisms involved in PTSD symptoms?

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The dream of trauma-related nightmares: Can physiological and subjective within-subjects  
measures help elucidate sleep-related mechanisms involved in PTSD symptoms?

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A Thesis in the Field of Psychology  
for the Degree of Master of Liberal Arts in Extension Studies

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## Abstract

Posttraumatic stress disorder (PTSD) poses significant challenges to individuals, impacting interpersonal relationships, work performance, and overall health outcomes. Treatment can be challenging due to the heterogeneity of PTSD, which is characterized by four distinct symptom clusters: intrusion, avoidance, negative cognition and mood (NegCog), and hyperarousal. Sleep disturbances, inherent to the intrusion and hyperarousal symptom cluster criteria, pervade all clusters. Interventions targeting daytime symptoms offer limited relief for nighttime disturbances, while interventions addressing sleep disruptions appear promising for alleviating both daytime and nighttime symptoms of PTSD. This study aims to elucidate sleep disruption differences across heterogeneous PTSD symptom clusters to inform personalized therapeutic approaches.

The data were generously contributed from a larger study in Dr. Edward Pace-Schott's lab examining sleep measures and different prolonged exposure therapy exposure stimuli in a population of trauma-exposed individuals. The variables included in the analysis fall into four categories: (1) sleep architecture, quality, and continuity measures; (2) daytime and sleep measures of arousal; (3) spectral power sleep measures; and (4) self-report assessment measures. These were analyzed in relation to both symptom cluster severity and cluster membership (based on symptom cluster questions in which each participant scored the highest). Additional exploratory analyses using multidimensional scaling (MDS) and investigating relationships between REM density (REMD) and spectral power were conducted.

Despite numerous observed trends, few correlations and pairwise comparisons achieved statistical significance after correcting for multiple comparisons in the main analyses. Significant differences were observed in sleep architecture, quality, and continuity measures. There was a notable association between total sleep time and intrusion cluster scores. In pairwise comparisons, the hyperarousal cluster displayed significantly higher mean scores on the Insomnia Severity Index (ISI) compared to the avoidance and intrusion cluster; the avoidance cluster also had a significantly higher mean ISI scores compared to the intrusion cluster. Both the avoidance and hyperarousal clusters exhibited higher mean Pittsburgh Sleep Quality Index (PSQI) scores than the intrusion cluster. The avoidance cluster also demonstrated significantly longer mean sleep onset latency (SOL) compared to the hyperarousal cluster.

These findings underscore the importance of examining nuanced PTSD-related sleep disruptions from a dimensional, symptom-based perspective. Despite the modest sample size, notable relationships between sleep patterns emerged depending on cluster membership and cluster symptom severity. The findings suggest hyperarousal symptoms may manifest in sleep maintenance issues, while intrusion symptoms may correlate with difficulties initiating sleep. Future research with larger cohorts is warranted to fully discern these associations, potentially paving the way for targeted interventions that ameliorate both daytime and nighttime PTSD symptoms.

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## Chapter I.

### Introduction

Posttraumatic stress disorder (PTSD) affects ~28 million people in the US alone, and the average person has an 8.7% lifetime risk of developing PTSD (Kessler et al., 2005). Individuals with PTSD often suffer from chronic debilitating interpersonal and occupational challenges due to its adverse emotional and psychological consequences (Kessler, 2002). Neurodegeneration, accelerated aging (Miller & Sadeh, 2014), and an increased risk of chronic disease (Kubzansky et al., 2007; Roberts et al., 2015) are associated with PTSD. According to data from the National Comorbidity Survey, PTSD is highly comorbid with several mental illnesses, including depression (~50%), alcohol misuse (~30%), phobia (~30%), and conduct disorder (~25%; Kessler, 2002). Given its prevalence and significant negative impact on individuals' quality of life, novel efficacious treatments for PTSD are needed.

### The Heterogeneous Nature of PTSD

The heterogeneous nature of PTSD can pose a challenge for treatment. The DSM-5 follows a 4-factor model of symptom clusters, including (1) intrusion, (2) avoidance, (3) negative alterations in cognition and mood (NegCog), and (4) hyperarousal (Blevins et al., 2015). Each symptom cluster may even have unique neurobiological correlates (Ragen et al., 2015), suggesting that differences between these groups are likely both behavioral and biological. Following a potentially traumatic event, the type of DSM-5 cluster symptoms an individual presents can predict susceptibility to developing PTSD

and symptom severity (Marqueses et al., 2023). This indicates meaningful differences between PTSD symptom clusters. Growing evidence underscores the need for transdiagnostic approach to PTSD research, rather than attempting to treat it as a unitary disorder (Biehn et al., 2013; Contractor et al., 2018, 2020; Forbes et al., 2020; Levin-Aspenson et al., 2021; Marshall et al., 2019). Experts in the field advise studying symptomology rather than a categorical diagnosis in order to enable more personalized and efficacious treatments (Ragen et al., 2015).

### PTSD in Relation to Sleep

An important relationship exists between sleep and the pathogenesis and persistence of PTSD symptoms (Germain, 2013; Pace-Schott et al., 2015; Saguin et al., 2021). Some authors have even suggested that at its core, PTSD might principally be a disorder of sleep-governing mechanisms (Ross & Sullivan, 1989). Sleep disturbance and increased insomnia are associated with increased PTSD symptom severity, and insomnia symptoms before and after a traumatic event predict PTSD symptoms (Gehrman et al., 2013; Neylan et al., 1998; Plumb et al., 2014; Wright et al., 2011). The interplay is likely cyclical, with sleep disturbance serving as a diathesis for PTSD, triggered by exposure to trauma, which subsequently exacerbates sleep quality issues, thereby heightening PTSD symptoms and maladaptive responses to trauma (Bryant et al., 2010; Cox et al., 2017; Goldstein & Walker, 2014; Koffel et al., 2013; Pace-Schott et al., 2012, 2015; Pigeon et al., 2013).

The quality of sleep not only impacts the mood and overall quality of life for individuals with PTSD, but it is also associated with decreased efficacy of therapeutic interventions, such as trauma-focused therapy (Kartal et al., 2021; Sullan et al., 2021). A

study on prolonged exposure (PE) therapy in veterans and active-duty personnel with PTSD revealed that while PE therapy improved daytime PTSD symptoms, it did not alleviate nighttime symptoms like insomnia or nightmares (Belleville et al., 2011; Walters et al., 2020). In contrast, interventions targeting sleep have been efficacious in reducing both sleep disturbances and daytime PTSD symptoms, with improvements in insomnia symptoms predicting improvements in overall PTSD symptoms (Galovski et al., 2016; Germain et al., 2007; Krakow et al., 2001; Moore & Krakow, 2007; Talbot et al., 2014; Walters et al., 2020).

The relationship between sleep disturbances and heterogeneous PTSD symptom clusters may vary bidirectionally; for example, insomnia appears to have a greater impact on intrusion compared to avoidance or hyperarousal symptoms, likely due to the role of sleep in memory consolidation (Cox et al., 2018). It has also been shown that poor sleep quality and reduced sleep efficiency is associated with increased negative affect (Short et al., 2017), potentially exacerbating daytime NegCog symptoms. Mounting research is revealing significant differences between PTSD symptom clusters in both subjective and objective sleep measures (Babson et al., 2011; Brownlow et al., 2022; Cox et al., 2018; de Boer et al., 2020; Denis et al., 2023; Gibson et al., 2019; Mellman et al., 2007; Van Wyk et al., 2016). These findings suggest the involvement of distinct mechanisms in cluster-specific sleep disturbances — and potentially, their effects on daytime symptoms. Given the efficacy of sleep interventions in ameliorating daytime PTSD symptoms, alongside the sleep-related differences between PTSD symptom clusters, a deeper understanding of cluster-specific sleep characteristics holds promise for developing novel, personalized PTSD treatment and prevention strategies.

## Background of the Problem

This section will delve into various aspects related to sleep, including measurement techniques and the significant role it plays in overall health and well-being. It will explore how sleep patterns are disrupted in PTSD, examining the intricate link between fear conditioning and sleep disturbances and underscoring their cyclical relationship with PTSD symptomatology.

### Quantifying the Architecture and Quality of Sleep

To understand sleep neurophysiology and its relationship with PTSD, it's first important to understand how sleep is measured. Since the late 1960s, polysomnography (PSG) has been instrumental in "pulling back the curtain" on the slumbering mysteries of sleep (Pace-Schott, 2009). PSG is comprised of measures of electroencephalography (EEG), electrooculography (EOG), and electromyography (EMG); EEG measures the fluctuating electrical potentials originating from the underlying cortex, EOG measures the proximity of the electronegative retina to the electrode, and EMG measures the tone of skeletal muscles (Pace-Schott, 2009). These three measures are visually inspected by experts to identify and score sleep stages using a method first developed by Alan Rechtschaffen and Anthony Kales in 1968 (Rechtschaffen & Kales, 1968; later revised by the American Academy of Sleep Medicine).

Frequency, amplitude, and morphology of brain waves are key differentiators of the different sleep cycles. These are captured by EEG, which measures the variation in membrane potentials summed across large numbers of cortical neurons under the electrodes used for recording; these fluctuations are what is referred to as 'brain waves.' Frequency (measured in cycles per second or Hertz [Hz]) signifies the speed of



fluctuation in electrical potential between successive peaks or troughs of EEG brain waves, while amplitude (measured in micro-volts) denotes the magnitude of potential change between these peaks and troughs; morphology, encompassing the shape of specific EEG waves or groups, reflects both frequency and amplitude, exhibiting characteristic forms like sleep spindles or K-complexes (Pace-Schott, 2009).

Another approach to measuring sleep is called activity-based sleep-wake monitoring, or actigraphy (Sadeh, 2011). Although it has lower specificity than PSG, the validity and reliability of actigraphy is reasonable for assessing sleep quality (Sadeh, 2011). Some of the benefits of actigraphy include lower cost and higher accessibility, making it easier to record more nights of sleep (Lam et al., 2023).

Sleep: What is it, and What is it Good For?

Nearly all animals experience sleep, and universally shared features of sleep include (1) increased threshold to sensory stimulation, (2) reduction in metabolism, (3) decreased motor output, (4) rapid reversal (unlike coma or hibernation), (5) lower homeostatic compensation, and (6) deprivation results in behavioral deficits (Campbell & Tobler, 1984).

There are four major phases of sleep, which are each distinguished by unique frequency, amplitude and morphology of brain waves, as well as muscle tone (Pace-Schott & Hobson, 2013).

1. Stage I non-rapid eye moment (NREM; N1)
  - a. Characterized by slow eye movements.
  - b. Brain wave frequency decreases from wake (Beta and Gamma) to eyes closed (Alpha) until Theta rhythm predominates.

2. NREM 2 (N2)
  - a. Marked by continued slowing of brain waves to predominantly within the Theta range (4-7 Hz).
  - b. Introduces phasic wave forms, including (1) sleep spindles (phasic clusters of spikes at sigma frequency with waxing and waning morphology), and (2) K-complexes (phasic large upward followed by downward deflections in EEG wave).
3. NREM 3 (N3 or slow wave [SWS] or delta sleep)
  - a. Predominated by high amplitude delta (0.5-4.9 Hz) waves, continuing the pattern of decreasing frequency and increasing amplitude in NREM.
  - b. Slow oscillations (less than 1 Hz) exert an organizing effect on delta oscillations, sleep spindles, and K-complexes.
4. REM (Rapid Eye Movement or “Paradoxical sleep”)
  - a. Fast mixed-frequency EEG that resembles waking brain wave morphology.
  - b. Sometimes called "paradoxical sleep" because while EEG resembles the waking brain, electromyography (EMG) reaches minimum level (lowest level of muscle tone); this is referred to as “REM Atonia.”

Starting from pre-sleep wake until the end of the NREM stages, there is a progressive decrease in the frequency of brain waves and a progressive increase in amplitude. Phasic features are introduced in the second phase of NREM sleep, including

sleep spindles and K-complexes (Pace-Schott & Hobson, 2013). Sympathetic outflow decreases from wake to NREM, and parasympathetic outflow becomes predominant during SWS; this means that heart rate, blood pressure, and respiration rate decrease during NREM and is characterized by pupillary miosis. Once the brain enters REM sleep, the frequency and amplitude "revert" to match the waking brain more closely. Sympathetic influence increases and homeostatic responses are attenuated. This cycle takes from 90-120 minutes, and therefore happens around four to five times per night — the cycle also changes throughout the night, with more SWS at the beginning and more REM towards the end.

It's widely believed that core functions of sleep help to remove waste from the glymphatic (pseudo-lymphatic perivascular network) system of the brain, conduct "housecleaning" in the brain through synaptic pruning, restore energy stores in the brain, perform an "emotional reset" with recalibration of systems involved in fear, stress, and reward, and to consolidate learning ("neuroplasticity") for later retrieval (Hobson & Pace-Schott, 2002). When parts of sleep are disrupted, especially during phases involved in emotional systems and memory, it can prevent these essential functions from occurring — and this is believed to play a key role in the pathogenesis and persistence of PTSD.

### Sleep and Emotional Regulation

The 'active systems consolidation' model of sleep-dependent memory consolidation outlines the process of memory consolidation during SWS (Klinzing et al., 2019). It involves a dialogue between the neocortex and hippocampus which transfers newly encoded memories to the neocortex for long-term storage. This process is facilitated by interactions between neocortical slow oscillations, thalamocortical sleep

spindles, and hippocampal ripples that generate spindle-ripple events; this is believed to be especially important for the integration of new experiences and the formation of stable memories, contributing to the overall memory consolidation process.

While SWS is important for episodic memory processing, it's been suggested that REM sleep is essential for the consolidation of emotional memories. The model of sleep-dependent emotional-memory processing, the *sleep-to-forget, sleep-to-remember* (SFSR) hypothesis (Goldstein & Walker, 2014; van der Helm & Walker, 2009), describes a process during REM sleep where an emotional experience becomes decoupled from the declarative memory and progressively removes the salience of the memory while keeping the memory itself intact (van der Helm & Walker, 2009). The SFSR hypothesis also posits that REM is a biologically ideal period for this “therapy-esque” process since noradrenergic activity is low to absent. This process would hypothetically allow a person to recall the memory without the associated original emotion. Further, it postulates that increases in limbic and paralimbic structures represent the phase-locking of ponto-geniculo-occipital (PGO) waves and theta oscillations, which serve to reactivate and integrate the emotional memory. In healthy individuals, this combination of processes would serve to strengthen the emotional memory without inducing sympathetic arousal (van der Helm & Walker, 2009).

Sleep processes elevate arousal associated with neutral stimuli while attenuating arousal associated with emotional stimuli; it's suggested that this enables both emotional and neutral stimuli to be accurately recalled, and prevent the type of maladaptive over-generalization seen in PTSD (Lipinska & Thomas, 2019). Sleep disruptions have been shown to interrupt this process: REM fragmentation, sympathetic activation, and greater

autonomic arousal during sleep is associated poorer accuracy in emotional memory recall (Lipinska & Thomas, 2019). These findings support the SFSR hypothesis and build upon it to demonstrate a convergent interaction between sympathetic activation, automatic arousal, REM fragmentation and emotional memory processing.

Sleep is also thought to promote emotional homeostasis through numerous processes, including anti-inflammatory mechanisms, hormonal regulation, neuromodulators, synaptic pruning, clearing of metabolites, and endogenous somnogens (Pace-Schott et al., 2015). Sleep disruption can lead to changes in biological function that may predispose individuals to PTSD; it has been demonstrated that following sleep deprivation, healthy young adults exhibit 60% greater magnitude in amygdala reactivity compared to the control group while viewing negative picture stimuli (Yoo et al., 2007). Collectively, these findings illustrate the multifaceted features of sleep that facilitate healthy emotional memory processing and homeostasis, while also highlighting the possible disturbances that could jeopardize these systems.

### Disruption of Sleep in PTSD

Nightmares are the most common symptom across all PTSD symptom clusters, and prevalence can be up to 100x higher in individuals with PTSD compared to the general population (Levin & Nielsen, 2009). Nightmares can have a significant influence on waking psychological distress, impair quality of life, and detrimentally affect sleep architecture (Elliott et al., 2020; Nielsen & Levin, 2007; Tanskanen et al., 2001). Nightmares can increase autonomic activation and fragment sleep (Blaskovich et al., 2020; Paul et al., 2019), create anxiety and avoidance of sleep (Pigeon & Gallegos, 2015), and negatively influence daytime mood (Köthe & Pietrowsky, 2001). Trauma-

related nightmares (TRNs) are nightmares that include trauma-associated emotions or content, and further intensify daytime feelings of threat and helplessness, hyperarousal, and sleep fragmentation compared to idiopathic nightmares (Wittmann et al., 2007).

Nightmares, a major form of sleep disturbance, are categorized as an intrusion symptom of PTSD, though they likely also relate bidirectionally to the other symptom clusters.

Nightmares can lead to consequential daytime distress, exacerbate both daytime and nighttime symptoms, and result in sleep fragmentation.

Beyond nightmares, individuals with PTSD are significantly more likely to experience sleep disturbances compared to trauma-exposed and healthy controls; the likelihood of difficulties initiating sleep is 4.8 times higher, disrupted sleep 4 times higher, and early morning awakening 5 times higher in individuals with PTSD (Ohayon & Shapiro, 2000). The same study found that 39.6% of individuals with PTSD met full DSM criteria for insomnia disorders, as compared to only 6.5% of individuals without PTSD. In fact, 70-90% of individuals with PTSD report experiencing sleep disturbances (Lam et al., 2023).

Increasing evidence underscores the significance of REM sleep in the symptomatology of PTSD. REM sleep is significantly more disrupted in individuals with PTSD compared to healthy controls (Breslau et al., 2004; Mellman et al., 2007; Ross et al., 1994). Measures of arousal during REM sleep were heightened in combat veterans who developed chronic PTSD (Ross et al., 1994). These findings are crucial, given the important role of REM sleep in the SFSR hypothesis and its link to nightmares (Mellman et al., 2007).

The field is still unravelling the anticipated bidirectional relationship between sleep disturbances and PTSD; it is likely cyclical with poor sleep predisposing individuals to PTSD, worsening after trauma exposure, and exacerbating PTSD symptoms (Pace-Schott et al., 2023).

### Fear Conditioning and Sleep

It has been proposed that fear conditioning and extinction are core facets of the relationship between PTSD and fragmented sleep (Pace-Schott et al., 2015; Rolls et al., 2013). Fear conditioning occurs when an association is learned between a neutral stimulus (NS; e.g., tone) and an aversive unconditioned stimulus (US; e.g., foot shock), where the NS becomes a conditioned stimulus (CS) once it evokes a conditioned fear response (CR) in the absence of the US. The opposing process is called fear extinction, wherein repeated exposure to the CS in safe contexts (i.e., no US) results in the creation of a fear-extinction memory that can inhibit the fear-conditioned memory. The fear-extinction memory is a new memory, and consolidation and generalization of the memory can be impeded by disrupted sleep. Research suggests that emotional memory processing and neurological activity in brain regions responsible for encoding and retrieval of fear conditioning/fear extinction memories occur during sleep (Genzel et al., 2015; Pace-Schott et al., 2012, 2015; Rolls et al., 2013). Relative to wakefulness, sleep has been shown to promote the retention and generalization of fear extinction learning (Pace-Schott et al., 2012). These findings implicate a positive feedback loop, initiated by exposure to trauma, between fear conditioning/extinction and sleep disruption in the pathogenesis, severity, and duration of PTSD (Pace-Schott et al., 2015; Saguin et al., 2021).

Neuroimaging studies that leverage fear and extinction paradigms have demonstrated that areas of the brain associated with fear conditioning, the amygdala and dorsal anterior cingulate cortex (dACC), and areas associated with formation of inhibitory extinction memories, the hippocampus and ventromedial prefrontal cortex (vmPFC), overlap with the anterior paralimbic REM activation area and reactivate during REM sleep (Nofzinger, 2004; Pace-Schott et al., 2015).

More research is needed to fully elucidate these relationships in individuals with PTSD, which will involve an exploration of deficient fear-extinction processes stemming from fragmented sleep and/or dysfunctional underlying neurocircuitry involved in sleep disturbance and PTSD.

### Measuring Features of Sleep in PTSD

This section will review various measures used to assess different dimensions of sleep, including (1) sleep architecture, quality, and continuity measures, (2) daytime and sleep measures of arousal, and (4) spectral power sleep measures. It will then examine how sleep measures exhibit heterogeneity across different PTSD symptom clusters, proposing links between specific types of disturbed sleep and distinct PTSD symptoms.

#### Sleep Architecture, Quality, and Continuity Measures

Sleep disruption, especially REM fragmentation due to heightened arousal during sleep, is believed to be central to the development, severity, and persistence of PTSD symptoms (Mellman et al., 1995; Raskind et al., 2003). Findings in rodent models support a reciprocal relationship between REM and emotion regulation: studies support that fear conditioning is linked to increased sleep onset latency (SOL), decreased REM



duration, fragmentation of REM periods, and increases in markers of alerting mechanisms analogous to rapid eye movements (REMs) in humans (Jha et al., 2005; Pawlyk et al., 2005; Sanford et al., 2003). PTSD-related disruptions to sleep architecture include decreased REM continuity and increased REM interruptions (lower REM%), more shifts from REM sleep to N1 sleep or wake, and overall more low-deep sleep (greater wake after sleep onset [WASO] and increase in N1 and N3 sleep; Babson et al., 2011; Brownlow et al., 2022; Cox et al., 2018; Mellman et al., 2007).

The noradrenaline (NA) plays a role in mediating arousal and enhancing emotional memories; in human studies, the secretion of NA is decreased in healthy controls during sleep, especially REM sleep, while levels may remain elevated in individuals with PTSD (Mellman et al., 1995). Interestingly, levels of NA in the urine were negatively correlated with measures of sleep quality and continuity, including total sleep time (TST) and sleep efficiency (SE; Mellman et al., 1995). A recent metaanalysis of human studies found overall greater SOL, lower TST, and lower SE in individuals with PTSD compared to healthy controls (although of these measures only SE reached statistical significance; Lam et al., 2023).

#### Daytime and Sleep Measures of Arousal

Heart rate variability (HRV), which can be measured as the variability of R-R intervals in ECG data, is believed to represent the balance of parasympathetic (PNS) and sympathetic nervous system (SNS) activity (Laborde et al., 2017; Shaffer & Ginsberg, 2017; Stein & Pu, 2012). The root mean square of successive differences in the R-R interval (RMSSD) serves as an indicator of PNS outflow; it reflects the vagus nerve's modulating effect on heart rate (Laborde et al., 2017; Shaffer & Ginsberg, 2017). A

recent pioneering study investigating HRV and PTSD symptomatology found that lower HRV during REM sleep is negatively associated with the severity of daytime PTSD hyperarousal cluster symptoms (Daffre et al., 2022). Studies conducted during both sleep and wake have demonstrated a negative correlation between HRV and PTSD severity — and a number of studies showed that trauma-exposed controls had higher HRV-measured PNS activity compared to individuals with PTSD (Ge et al., 2020; Rissling et al., 2016; Schneider & Schwerdtfeger, 2020; Ulmer et al., 2018).

REM density (REMD), the number of rapid eye movements during sleep, has historically been linked to dream intensity, as higher number of REMs were seen in “active” compared to “passive” dreams (Berger & Oswald, 1962). However, a recent study found that REM fragmentation rather than REMD was related to severity of TRNs (Habukawa et al., 2018). More recently, it has been suggested that REMD be considered a biomarker of arousal, and a useful tool in disorders involving autonomic dysfunction, such as PTSD (Barbato, 2023; Saleh et al., 2022). REMD is higher in patients with PTSD compared to healthy controls and patients with major depressive disorder (MDD) (Habukawa et al., 2018; Kobayashi et al., 2007; Mellman et al., 1995). REMD has differing relationships with disorders that share symptoms with PTSD symptom clusters; it is increased in MDD patients, but not panic disorder patients, compared to healthy controls (Lauer et al., 1992).

Daytime PTSD symptom severity is positively associated with a greater number of sleep disruptions (Schenker et al., 2023). The relationship is reciprocal, with sleep disruptions in turn being associated with greater daytime PTSD symptom severity, especially number of intrusions (Kartal et al., 2021). Skin conductance response (SCR) is

an output of the SNS, and is significantly correlated with the probability of developing chronic PTSD (Hinrichs et al., 2019). It has been suggested that SCR may be a useful biomarker of PTSD symptom severity, which could be helpful for investigations into relationships between sleep and daytime PTSD symptoms (Grasser et al., 2022).

### Spectral Power Sleep Measures

As mentioned earlier, failure in fear extinction memory consolidation plays an important role in PTSD-related trauma memories (Goldstein & Walker, 2014; Pace-Schott et al., 2023). Emotional memory processing is thought to take place mainly during REM sleep (Goldstein & Walker, 2014; van der Helm & Walker, 2009), and it has been hypothesized that PTSD-related REM disturbances may prevent the FE memories from persisting and generalizing (Pace-Schott et al., 2023; Richards et al., 2020; Ross & Sullivan, 1989).

An increasing body of evidence supports a connection between the processing of affective memory and theta oscillations in limbic and prefrontal regions (Cowdin et al., 2014; Jones & Wilson, 2005; Paré et al., 2002). Prefrontal theta power during REM is significantly correlated with sleep-dependent facilitation of emotional memory (Nishida et al., 2009). It has also been shown that theta activity during REM drives higher amplitude PGO waves (mentioned as part of the SFSR hypothesis), further supporting its role in the processing of emotional memories (Hutchison & Rathore, 2015).

Increased gamma frequency power is linked to emotionally arousing stimuli that induce emotional memory via cortical arousal — and this process may facilitate the encoding and expression of emotional memories (Headley & Pare, 2013). It has also been shown that gamma band power in frontal-central and posterior regions is significantly

negatively correlated with anxiety (as measured by a Korean version of the State-Trait Anxiety Inventory; Kim et al., 2022). Frontal gamma was found to be significantly higher in patients with PTSD compared to individuals with anxiety disorders, suggesting that gamma can be a useful biomarker of PTSD and that it has potentially unique relationships with different PTSD symptomatology (Moon et al., 2018).

High frequency power in the beta range has been linked to nightmares, REM sleep state continuity, and subjective insomnia (Mellman et al., 2007). Beta power is also associated with reduced PTSD symptoms and greater subjective ability to regulate emotions, suggesting their role in emotional processing during sleep (Denis et al., 2021).

PTSD is associated with increased higher frequency power in the beta and gamma frequency range (>20 Hz) during REM and NREM sleep, and trauma-exposed individuals who do not develop PTSD have been shown to have higher REM theta power compared to those that do develop PTSD (Cowdin et al., 2014). These findings support spectral power frequencies as measures of emotional memory processing and arousal during REM sleep.

#### Heterogenous Clusters and Heterogeneous Sleep

Studies show distinct patterns of sleep disruptions linked to the severity of PTSD symptom clusters. A recent study examined the relationships between PSG measures and three PTSD symptom clusters, including avoidance, intrusion, and hyperarousal. (Brownlow et al., 2022). The study found that higher levels of N1 and N2 sleep, along with reduced TST, positively correlated with symptom severity across all three clusters. Intrusion and hyperarousal symptom clusters were negatively associated with SE and total REM sleep, while avoidance and hyperarousal were positively associated with

greater REM latency (REML). In another study, it was observed that intrusion cluster symptoms were linked to challenges in initiating and maintaining sleep, as well as nightmares (Babson et al., 2011). Hyperarousal cluster symptoms, on the other hand, were only associated with nightmares and difficulty in maintaining sleep. Notably, avoidance cluster symptoms did not show significant associations with any of these sleep disturbances. The results contradict the author's initial hypothesis that symptoms of avoidance would be associated with difficulties in initiating sleep. This hypothesis was based on the association between insomnia symptoms and fear of sleep in PTSD, which could result in avoidance of sleep (Werner et al., 2021). The link between intrusion and difficulty initiating sleep is supported by research indicating that intrusion cluster symptoms are linked with increased rumination, which has been shown to increase SOL (Zoccola et al., 2009). The findings indicate that varying degrees of symptoms across different PTSD symptom clusters may be related to distinct patterns of sleep disruptions.

Subjective measures of sleep quality also differ across symptom clusters. One study using the Posttraumatic Diagnostic Scale (PDS) found that intrusion symptom severity and arousal had the highest correlations with the Disturbing Dream and Nightmare Severity Index (DDNSI) and Insomnia Severity Index (ISI), while avoidance symptom severity had lower correlations with both (Krakow et al., 2004). Additionally, the Functional Outcomes of Sleep Questionnaire was most highly correlated with the arousal cluster and avoidance cluster and was only weakly correlated with the intrusion cluster. PTSD patients with greater hyperarousal symptom severity are also more likely to self-report poorer sleep quality (van der Helm et al., 2011). These findings demonstrate

that there are not only physiological differences based on symptom severity, but also differences in perceived sleep quality.

The research supports links between PTSD cluster symptoms and insomnia. It has been suggested that insomnia may be linked to hyperarousal symptoms through increased SNS activation, as measured by HRV (Castro-Diehl et al., 2016). Insomnia symptoms have also been shown to specifically exacerbate intrusion symptoms, but not the severity of avoidance or hyperarousal cluster symptoms (Cox et al., 2018). It's hypothesized that this relationship is due to sleep's role in healthy emotional memory consolidation (Cox et al., 2018; Goldstein & Walker, 2014).

These studies paint an interesting picture of relationships between the severity of PTSD clusters and disturbances in sleep quality and architecture. Research has overwhelmingly focused on the association between PTSD hyperarousal symptoms and sleep (Blaskovich et al., 2020; Bonnet & Arand, 2010; Daffre et al., 2022; Mellman et al., 1995; Oliver et al., 2020; Van Wyk et al., 2016), while no study was found that investigates the NegCog cluster. Further, there remains a paucity of research looking at symptom cluster severity in relation to a battery of both subjective and objective sleep-related variables involved in PTSD-related disordered REM arousal and emotional memory processing, especially within one group of individuals. Investigating waking- and sleep-related biomarkers from a dimensional, symptom-based approach may help to clarify distinct relationships between sleep and PTSD symptom clusters — and help to develop novel, individualized treatment interventions.

## Research Aims, Goals, and Hypotheses

The original study was a within-subject design spanning 2 weeks in trauma-exposed individuals who experience frequent trauma-related nightmares (Pace-Schott, 2020). After each nightmare-induced awakening, participants were instructed to create a time-stamped audio recording of their nightmare. Ambulatory PSG was recorded during four nightmare nights for later sleep physiology analysis. A script was created for a later script-driven imagery (SDI) session based on a sufficiently long and index-trauma-associated sleep diary entry. Each entry detailed a participant's self-reported experiences regarding the salience and content of a nightmare, as well as their sleep quality.

Participants went into the laboratory for two sittings. They underwent 5 intervals of randomly ordered trauma or nightmare SDI with neutral breaks in between. The entire process lasted roughly three hours.

A group of 40 participants were recruited to the study, based on preliminary findings from similar studies conducted in the labs of Dr. Ivkovic and Dr. Pace-Schott. Of the originally recruited participants, 25 completed at least some portion of the protocol and 17 completed all aspects (including SDI) of the protocol. The main inclusion criterion was that individuals experienced a potentially traumatic event and frequent trauma-related nightmares. Some participants had partial PTSD, while others met full criteria. It is important to note that while the original study was conducted for a grant, the collected data were analyzed here to answer unique questions that were not included in the original study proposal.

The present study leverages the Research Domain Criterion (RDoC) framework approach (Insel et al., 2010), which involves a dimensional examination of a particular population across a spectrum of both typical and atypical values for specific symptoms.

Specifically, this research focuses on adults recently exposed to trauma, exploring a continuum of sleep quality and four PTSD symptom cluster severity variables within this population.

The goal of this research is to contribute to a more in-depth understanding of the sleep-wake underpinnings of PTSD symptom clusters; this could potentially provide insights into the pathophysiology, prevention, and treatment not only of PTSD itself but other adjustment and stress-related disorders, as well. Investigating the physiological and subjective measures related to sleep disturbances and emotional memory processing in PTSD may provide insights into the resistance of nighttime symptoms to daytime therapeutic interventions. Lastly, future studies building on these findings could potentially elucidate which underlying mechanisms may help to improve and prevent PTSD- and stress-related symptoms.

#### Aim 1: Investigate Sleep Architecture, Quality, and Continuity Measures

This aim explores potential relationships between PTSD symptom clusters and objective and subjective measures of sleep architecture, quality, and continuity. Objective measures include Sleep Efficiency (SE), Sleep Onset Latency (SOL), REM Latency (REML), Total Sleep Time (TST), number of REM Periods (#REM), and wake after sleep onset (WASO). Subjective measures include the Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI).

Hypothesis 1. It is expected that there will be a negative and more pronounced correlation between hyperarousal cluster symptoms and sleep architecture, quality, and continuity measures, especially in relation to sleep maintenance (SE, TST, WASO). Intrusion cluster symptoms are also expected to be highly negatively correlated with sleep quality



measures, given their relationship with nightmares, as well as measures of sleep maintenance (SOL, SE, TST, #REM, WASO). NegCog and avoidance symptoms are expected to exhibit smaller negative correlations with these sleep measures.

Given that this population was recruited based on reports of trauma-related nightmares, a negative correlation between all PTSD-cluster symptoms and ISI and PSQI is predicted.

#### Aim 2: Examine Daytime and Sleep Measures of Arousal

This aim focuses on investigating associations between cluster symptoms and measures of arousal during sleep, including rapid eye movement density (REMD), REM sleep heart rate variability (HRV), and change in skin conductance response (SCR) from baseline to during the neutral SDI (SCR neutral) and trauma/nightmare SDI sessions (SCR negative).

Hypothesis 2. Hyperarousal cluster symptoms are anticipated to have a positive correlation with REMD and a negative correlation with REM HRV, indicating heightened physiological arousal during sleep. NegCog score is expected to be positively associated with REMD and negatively with REM HRV, to a lesser degree than hyperarousal. Significant correlations are not expected between intrusion and avoidance cluster symptoms and the measures of arousal.

#### Aim 3: Spectral Power Sleep Measures.

The objective of this aim is to examine affective memory processing during sleep, measured as levels of frontal gamma, beta, and theta power during REM. These neural oscillations will be investigated in relation to the PTSD clusters.

Hypothesis 3. It is hypothesized that hyperarousal cluster symptoms will exhibit the most substantial negative correlation with theta, beta and gamma power, reflecting a more pronounced impact on sleep-related affective memory processing compared to the other PTSD symptom clusters.

#### Aim 4: Self-Report Assessment Measures

This aim involves the exploration of mental health assessments, including the State-Trait Anxiety Inventory (STAI-T), Quick Inventory of Depressive Symptomatology (QIDS), and the Morningness-Eveningness Questionnaire (MEQ). The goal is to discern how scores on these assessments correlate with the PTSD symptom clusters, and the differences between the symptom clusters.

Hypothesis 4. The QIDS scores are expected to exhibit the most pronounced positive correlation with NegCog cluster symptoms, while hyperarousal cluster symptoms are expected to demonstrate the highest positive correlation with scores on the STAI-T.

## Chapter II.

### Methods

This section will detail participant recruitment and demographics, the experimental protocol, the collection and computation of measures, and the clinical assessments conducted.

#### Participants

A mixed-sex sample of community volunteers experiencing frequent TRNs were recruited for the study. Individuals were recruited from the community via social media with advertisements directed to the greater Boston area (Facebook) and trauma-related interest groups (Reddit), electronic bulletin boards at local universities, and Mass General Hospital research participation sites.

Participant candidates were evaluated on a case-by-case basis to determine if they reported frequent trauma-related nightmares as well as symptoms of PTSD. Participant candidates first completed a phone screening based on a full list of inclusion and exclusion criteria. Following a successful phone screening, participant candidates underwent psychiatric and sleep disorders interviews using Structured Clinical Interview for the DSM-5 (SCID-5; First et al., 2016) and the Clinical Interview for DSM-5 Sleep Disorders Module (SCISD; Taylor et al., 2018) and were screened for suicidality using the Columbia-Suicide Severity Rating Scale (C-SSRS; Katz et al., 2020). They were screened for PTSD symptomatology with the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5; Weathers, Blake, et al., 2013), Life Events Checklist (LEC; Gray et al., 2004) and the PTSD Checklist for DSM-5 (PCL-5; Weathers, Litz, et al., 2013).

Additional questionnaires were completed using MGH online Research Electronic Data Capture (REDCap™) system (© 2013 Vanderbilt U.) including the Childhood Trauma Questionnaire (CTQ; (Bernstein et al., 2008), Trauma History Questionnaire (THQ; Hooper et al., 2011), Life Events Checklist for DSM-5 (Contractor et al., 2020), and Peritraumatic Distress Inventory (PDI; Brunet et al., 2001); 1. Pittsburgh Sleep Quality Index (Buysse, 1989) with PTSD addendum (Germain et al., 2005); 2. Insomnia Severity Index (Bastien, 2001); 3. Morningness-Eveningness questionnaire (Horne, 1976); 4. Spielberger State-Trait Anxiety Inventory (Spielberger, 1990); and 5. Inventory of Depressive Symptomatology (Rush, 2003). Inclusion criteria was a SCID-5-RV-based diagnosis of PTSD or partial PTSD (requisite number of symptoms in at least three of the four diagnostic clusters) and self-report of at least 2 nightmares per week related to a specific “index trauma” containing content similar to the original traumatic event. Exclusion criteria included: history of psychotic, bipolar-1 or autism spectrum disorders; risk to self or others; obstructive sleep apnea (OSA); neurological injury or disease; severe systemic disease; benzodiazepines, beta-blockers, prazosin or antipsychotics; current substance use disorder.

Of the 40 participants who consented to begin the study, 17 individuals completed all portions of the study. Characteristics of study completers are presented in Table 1, 2, and 3 below. The majority of participants were self-identified female (82%), white (70%), and single (82%).

Table 1. Sample Characteristics.

	<i>n</i>	%
Gender		
Female	14	82
Male	3	18
Race		
Asian	3	18
Black or African American	1	6
White	12	70
Prefer not to say/unreported	1	6
Marital status		
Single	14	82
Married	1	6
Divorced	1	6
Widowed	1	6

Table 2. Assessment Characteristics.

	<i>n</i>	<i>M</i>	<i>SD</i>	Min	Max
Age	17	27.31	10.64	19	54
PTSD severity					
Full PTSD diagnosis (CAPS-5)	10/17				
CAPS total	17	28.05	12.11	5	47
PCL-5 total	17	46.29	13.05	21	63
Psychopathology measures					
STAI-T total	16	48.63	12.25	27	72
QIDS-SR total	16	14.81	4.68	5	23
Sleep assessments					
ISI total	16	12.13	5.67	3	21
PSQI total	16	9.31	4.48	3	17
ESS total	16	6.94	4.07	0	13
MEQ total	16	48.13	10.10	24	62

*CAPS, Clinician Administered PTSD Scale; Higher score, greater PTSD symptoms. PCL-5, PTSD checklist (self-report); Higher score, greater PTSD symptoms. STAI-T, Spielberger Trait Anxiety Inventory; Higher score, greater trait and state anxiety symptoms. QIDS-SR, Quick Inventory of Depressive Symptomatology (self-report); Higher score, greater depressive symptom severity. ISI, Insomnia Severity Index; Higher score, more severe and disruptive insomnia symptoms. PSQI, Pittsburgh Sleep Quality Index; Higher score, poorer overall subjective sleep quality. ESS, Epworth Sleepiness Scale; Higher score, increased daytime sleepiness; MEQ, Morning Evening Questionnaire; Higher score, greater preference for mornings.*

Table 3. Sleep Characteristics.

	<i>n</i>	<i>M</i>	<i>SD</i>	Min	Max
Actigraphy measures					
Total sleep time (min)	13	413.48	81.32	297.92	528.44
Sleep onset latency (min)	13	32.82	14.44	13.21	57.73
Sleep efficiency (%)	13	88.03	5.71	77.25	94.51
Sleep physiology					
WASO	17	44.34	72.37	0.50	295.00
REML	17	162.00	99.79	51.00	341.00
REM%	17	23.64	10.92	5.10	46.50
N1%	17	5.71	2.81	2.00	12.10
N2%	17	68.51	10.99	50.60	89.90
N3%	17	2.16	4.17	0.00	13.50
REM HRV	16	41.08	20.32	13.30	81.40
REMD	16	4.69	2.55	1	9
SCR neutral	17	0.69	0.31	0.19	1.48
SCR negative	17	0.91	0.65	0.12	2.29

*WASO = wake after sleep onset. REML = REM Latency. REM% = percent of REM sleep. N1% = percent of N1 sleep. N2% = percent of N2 sleep. N3% = percent of N3 sleep. REM HRV = heart rate variability during REM sleep measured by RMSSD. REMD = REM density. SCR neutral = difference in SC from baseline to neutral SDI. SCR negative = difference in SC from baseline to nightmare/trauma SDI.*

## Procedure

The original, multi-phase study used a within-subjects quasi-experimental design. Participants completed 2 weeks of at-home sleep and nightmare diaries with time-stamped audio-recorded reports of dream content upon awakening from any nightmare. They wore a wrist actigraph throughout this period, completed two nights of ambulatory PSG, and answered online questionnaires. Participants' nightmare and original trauma reports were audio-recorded for use as scripts in an SDI protocol (McGrory et al., 2024, in review). The participants underwent two listening sessions on a single day, one with their nightmare script and one with their original trauma script. During these sessions, they wore a novel, wearable brain imaging and physiological monitoring device (NINscan; Strangman et al., 2018). Sessions were separated by 1 hour and script order (trauma vs. nightmare) were counterbalanced across participants.

### Ambulatory Polysomnography

During Phase I, participants underwent ambulatory PSG using the Somte-PSG ambulatory recorder (Compumedics USA, Inc., Charlotte, NC). Each sleep-stage (N1, N2, N3, REM) as a percent of TST and spectral power in 7 frequency bands within each sleep stage were included in the measures. REM-specific measures include REMD and REM HRV (Daffre et al., 2022; Mellman et al., 2004; Ulmer et al., 2018). An experienced research PSG technician scored sleep using AASM criteria. REMD was defined as the number of 3-s mini epochs containing rapid eye movements within a 30-s REM sleep epoch (Lechinger et al., 2021).



## Heart Rate Variability and Artifact Detection

European Data Format (EDF) files of whole-night PSG sleep recordings containing 25 channels (6 x EEG, 2 x EOG, 2 x Chin EMG, and ECG) were extracted using Profusion software. Only the second night PSG recordings were used here, except for one participant for whom the second night was not available. Corresponding hypnogram text files with 30-s epochs were used to calculate the start and end time for each sleep stage.

Files were imported to Kubios HRV premium software (Kubios Oy, Kuopio, Finland) for artifact correction and computation of time-domain and frequency-domain HRV parameters. In-house lab methods were followed for ECG signal processing and artifact correction. Start and end times for each REM period were inputted based on the corresponding hypnogram file. The built-in Kubios low-pass filter was used for baseline artifact correction. The built-in QRS detection algorithm was applied to automatically detect and mark R spike instants in the ECG data. A manual pass over all REM periods across all participants was done to identify artifacts, including extrasystoles, premature ventricular contractions, and ectopic beats, as well as missing or erroneous R spikes. The Kubios histogram distribution of RR intervals and pNNxx value, which represents the percentage of adjacent RR intervals differing by more than 50-ms (a measure of variability), were used to monitor overall data quality. Markers on ambiguous R spikes were removed only if it improved the pNNxx value by more than .2%. Because transition between sleep stages can disrupt quality at the beginning and end of each sample, these periods were removed upon visual inspection if there was unacceptable channel noise obscuring the R spikes, and trimming the data did not decrease the period to less than 5

minutes. An entire REM period was excluded from the HRV calculation if it was less than 5 minutes or if the Kubios medium filter removed >10% of heartbeats. A subject was excluded from analysis if they had no REM periods greater than 5 minutes (1 participant), or if there were more than 3 extrasystoles in a minute (indicating a cardiac issue). HRV calculations were produced for each participant using RR intervals across all REM periods weighted by length of REM period; HRV RMSSD and Frequency-Domain results were extracted for statistical analysis. A detailed analysis log contains a record of all manual changes to the ECG data in Kubios.

#### REM Density

REMD was calculated using the intersected output of three open source, validated REM detection algorithms (Vallat & Walker, 2021; Yetton et al., 2016). The EDF files containing left (LOC) and right (ROC) EOG channels of whole-night PSG sleep recordings taken from the Somte-PSG ambulatory recorder were extracted as previously described. The expertly scored hypnogram text files containing the epochs for each sleep stage were used to calculate the start time and end times for each REM period in Python using DataSpell (JetBrains, Prague, Czech Republic). The REM period, start time, end time, and participant ID were saved to a CSV file containing REM periods for all participants.

The YASA algorithm analysis was implemented in Python. Prior to running the YASA algorithm, the LOC and ROC data was transformed to standard units ( $\mu\text{V}$ ) and a Butterworth bandpass filter [0.3 Hz–5 Hz] was applied (Yetton et al., 2016) using a low filter order ( $N=1$ ) to avoid ringing and overshooting. The hypnogram data was imported from the CSV and up-sampled to match the sampling frequency of the EOG data (256

Hz). The YASA algorithm was then applied to the data, using an amplitude thresholding of the negative product of the LOC and ROC filtered signal to detect REMs. This thresholding approach is based on previous, validated methods of REM detection (Vallat & Walker, 2021). The algorithm parameters used minimum and maximum amplitudes for REM peaks of 50  $\mu\text{V}$  to 325  $\mu\text{V}$ , a minimum and maximum REM duration of 0.3 to 1.5 seconds, and a REM frequency rate of 0.5 to 5 Hz.

The Yetton Automatic REM Detector and Thresholding algorithms were applied using MATLAB (The MathWorks Inc., 2022. Optimization Toolbox version: 9.4 [R2022b], Natick, Massachusetts). The Automatic Rapid Eye Movement (REM) Detector algorithm is a validated, machine learning approach that predicts REMs based on 25 optimized features, including Amplitude, Width, Prominence, Rise and Fall Slope, Linear Variance, Cross Correlation, Discrete Wavelet Transform (DWT), Dynamic Time Warping (DTW), Coastline, Nonlinear Energy, Spectral Skew and Kurtosis, Delta Sleep Instability (DSI), Fast Sleep Instability (FSI), and Bidirectional Biased Distribution Index (BBDI). The Thresholding approach employs thresholding rules that intersect Amplitude, Slope, Cross-Correlation, and Discrete Wavelet Transform (DWT) to identify REMs. Both algorithms automatically apply a zero-phase digital bandpass filter from 0.3 Hz to 5 Hz with 40DB attenuation prior to REM detection.

Algorithm outputs for each participant were extracted into CSV files, and the mean value across all three was used as the REMD value for each participant.

### Calculating Bandpower Frequencies

The YASA (Yet Another Spindle Algorithm) toolbox, developed in Matthew Walker's lab, was also used for the calculation of bandpower frequencies (Vallat &

Walker, 2021). This process was fully executed in Python. The YASA toolbox is specifically designed to analyze and extract information from PSG data, and the EDF files of whole-night PSG sleep recordings and hypnogram files used for REMD and HRV calculations were used for the bandpower frequency calculation. The YASA toolbox extracts relevant features from the EEG signal and uses Fast Fourier Transform to calculate the spectral powers of different frequency bands, including delta, theta, alpha, beta, and gamma for each sleep stage. Frequencies were visually inspected and a bandpass filter between 0.5 - 45 Hz was applied before bandpower frequency calculation.

#### Skin Conductance Response

Physiological biosignals were gathered using the Biopac MP150 system (Biopac Systems Inc. in Goleta, CA) coupled with AcqKnowledge 4.1.5 software and ECG100C, EMG100C, and EDA100C transducer modules for recording heart rate (HR), electromyography (EMG), and skin conductance (SC). The sampling rate for these physiological biosignals was set at 2000 Hz. For measuring SC, two 11 mm Ag/AgCl disposable electrodes (Biopac EL507) filled with isotonic paste (Biopac Gel 101) were affixed to the hypothenar surface of the participant's nondominant hand, with a separation of 14 mm between them. Mean SC levels during the baseline period were subtracted from the respective levels during the SCR periods recorded during the neutral and trauma/nightmare SDI periods. Subsequently, these change scores underwent square root transformation to mitigate heteroscedasticity, and negative signs were retained following the calculation of the square root of absolute values. The values used in these analyses are relative change in SC from baseline to either neutral SDI (SCR neutral), or from baseline to the nightmare or trauma SDI (SCR negative). Specifically, a 30-s baseline mean

preceding each script was subtracted from the maximum during a 30-s imagery period immediately following listening to a script (McGrory et al., 2024, in review).

### Clinical Measures

Listed below are the clinical measures included in the study and the corresponding analyses. Each description outlines the construct being assessed, along with the range of the scale and interpretation of higher or lower score on each.

#### Clinician Administered PTSD Scale for DSM-5 (CAPS-5)

CAPS-5 is the clinician administered “gold standard” assessment for PTSD (Weathers et al., 2013). A 5-point severity scale ranging from 0 (absent) to 4 (extreme / incapacitating) is used to assess severity of the 20 DSM-5 symptoms of PTSD. PTSD severity was measured by total score, which can range between 0 and 80.

#### PTSD Checklist for DSM-5 (PCL-5)

A self-report measure with 20 items assessing the 20 DSM-5 symptoms of PTSD (F. W. Weathers, Litz, et al., 2013). Each item is rated on a Likert scale from 1 (not at all) to 5 (extremely), and a cutoff score of 31-33 indicates probable PTSD. PCL-5 symptom cluster groups include intrusion (items 1-5), avoidance (items 6-7), negative affect (items 8-14), and hyperarousal (items 15-20).

### Quick Inventory of Depressive Symptomatology (QIDS-SR)

A 16-item self-report measure of depression symptom severity that correlate with the nine DSM-IV symptom criterion domains; scores range from 0 to 27 (Rush et al., 2003).

### Spielberger State Anxiety Inventory (STAI-T)

A 40-item self-report assessment for measuring state and trait anxiety (Spielberger et al., 1983). 20 items assess state anxiety, and 20 items measure trait anxiety. A 4-point scale is used for rating each item from 1 (almost never) to 4 (almost always).

### Insomnia Severity Scale (ISI)

A brief, validated, self-report measure of an individual's perception of their symptoms and daytime consequences of insomnia, and the amount of distress/concern caused by these symptoms (Bastien, 2001). It includes 5 items, each rated on a scale from 1 (not at all) to 4 (very much). Scores range from 0 to 28.

### Pittsburg Sleep Quality Index (PSQI)

A self-report assessment covering a 1-month period that measures subjective aspects of sleep quality (Buysse et al., 1989). Questions cover subjective sleep quality, disturbances, sleep onset latency, total sleep time, sleep efficiency, sleep-related medications, and daytime dysfunction.

### Epworth Sleepiness Scale (ESS)

A self-report questionnaire measuring daytime sleepiness as chance of dozing off while engaged in activities (Johns, 1991). It includes 8 items, each representing an activity, scored on a 4-point scale from 1 (would never doze) to 3 (high chance of dozing).

### Morningness-Eveningness Questionnaire (MEQ)

A 19-item self-assessment used to identify individuals' chronotype: morningness, eveningness, or intermediate (Horne & Ostberg, 1976). Items measure morningness-eveningness in human circadian rhythms by evaluating preferred times for sleep, wake, and activities. A higher total score represents a preference for mornings.

## Chapter III.

### Results

This section describes and presents the statistical analyses. It first explores the internal consistency of the PCL-5 and potential score biases across symptom clusters. Then it discusses the results, addressing the study's four primary aims followed by two exploratory analyses.

#### Statistical Analysis

All analyses were done in R using RStudio Version 2022.12.0+353. PCL-5 questions were grouped into four clusters aligned with the DSM-5 symptom groups; questions 1-5 relate to intrusion symptoms, 6-7 avoidance, 8-14 negative affect, and 15-20 hyperarousal (Weathers, 2013). In line with similar studies, the total cluster scores for each participant represent symptom severity (Brownlow et al., 2022). The intrusion cluster questions on the PCL-5 are comprised of items related to intrusive thoughts and memories. The avoidance cluster focuses on avoidance behaviors and efforts to numb or avoid reminders of the traumatic event. The NegCog cluster reflects changes in thought patterns and mood associated with the traumatic event. The hyperarousal cluster addresses symptoms of heightened arousal and reactivity to stimuli associated with the traumatic event. Since participant eligibility included frequent TRNs and sleep disturbance, a sensitivity analysis removing question 2 (“Repeated, disturbing dreams of the stressful experience”) and question 20 (“Trouble falling or staying asleep”) was conducted; results did not change significantly and therefore both questions remain in the



analyses. Cronbach's  $\alpha$  was calculated for total PCL-5 score and each of the symptom question clusters.

Separately, using a symptom-cluster based approach, participants were partitioned into a Top PCL-5 Cluster (TPC) based on the cluster questions in which they had the highest mean score. For example, a participant whose highest mean score was in the intrusion cluster questions would be in the intrusion TPC (TPC<sub>Int</sub>). The other TPCs refer to the hyperarousal cluster questions (TPC<sub>Hyp</sub>), avoidance questions (TPC<sub>Avo</sub>), and NegCog questions (TPC<sub>Neg</sub>). As shown later, there were significant differences in overall PCL-5 score based on TPC membership, suggesting that overall scores may be skewed based on an individual's primary symptoms. Therefore, PCL-5 scores were normalized to have a mean of zero, and TPC was used for all non-numerical analyses (linear regression, cluster pairwise differences, and multidimensional scaling).

Spearman's correlation was used to estimate rank-based associations between all paired combinations of physiological and subjective measures and was corrected for multiple comparisons using the False Discovery Rate (FDR) adjustment (Best & Roberts, 1975). Spearman's method was well-suited since it does not assume the data necessarily come from a bivariate normal distribution. Linear regression models were used to estimate linear relationships between TPC membership and three physiological outcome variables, including REM HRV, REMD, and theta power. All models generally adhered to the assumptions of linear regression and no variables required transformation.

Multidimensional scaling (MDS) was used for exploratory analysis; it is a dimensionality reduction technique akin to Principal Component Analysis (PCA). The objective of MDS is to map high-dimensional data onto a 2-dimensional (2D) plane in

order to visualize and analyze relationships between variables in a more interpretable format (Borg et al., 2020). MDS is like creating a 2D constellation map from star positions; each star's position represents its relative distance and orientation from other stars, analogous to dissimilarities between data points in MDS. Overlaying additional information, such as star brightness or constellation boundaries provides further context and insight into the celestial landscape. In the context of this study, dissimilarities between data points reflect attributes of the subjects. Therefore, two subjects with significant differences in sleep measures would be positioned farther apart in the 2D space. Coloring the MDS solution by TPC membership creates a visual representation of how well subjects with similar sleep patterns align with symptom cluster membership.

In MDS, distances between data points in space are calculated by an algorithm that minimizes a "loss function" known as Stress (Borg et al., 2020). Stress quantifies the discrepancy between the actual distances (dissimilarities) and the observed proximities of objects. The goal of the algorithm is to minimize this discrepancy, ideally reducing it to zero, thereby achieving an optimal solution where distances precisely reflect dissimilarities. Since the order of much of this study's data was interpretable, an ordinal MDS model was employed, aiming to maximize the alignment between the order of distances and the order of the data. Two ordinal 2D MDS configurations were computed in these analyses using the use the R-package SMACOF. The two computed 2D MDS configurations of subjects were based on physiological and subjective measure similarities; no TPC information was included.

Support Vector Machines (SVMs) are a powerful class of supervised learning algorithms that find the optimal hyperplane in the input space to separate different

classes, maximizing the margin between the hyperplane and the nearest data points, known as support vectors. After computing the MDS configurations, a linear SVM classifier attempted to categorize subjects within the MDS configuration space into the four TPCs. SVM classification accuracy sheds light on the alignment between the MDS configuration measures and TPC membership.

The first MDS configuration was employed to explore the clustering patterns among subjects based on a set of variables related to sleep physiology, including measures of sleep architecture, autonomic nervous system activity, and demographic variables where appropriate. Specifically, #REM, REMD, REM HRV, TST, SOL, SE, SCR neutral, SCR negative, and age were added to the MDS solution. Subsequently, the SVM classifier described above was applied, attempting to categorize subjects into TPC<sub>Avo</sub>, TPC<sub>Hyp</sub>, TPC<sub>Int</sub>, or TPC<sub>Neg</sub>.

A second MDS configuration included only subjective measures. This set of variables included ISI, PSQI, ESS, MEQ, STAI-T, and QIDS scores. Following the MDS analysis, the same SVM approach attempted to categorize participants into clusters, corresponding to their TPC membership.

### PCL-5 Symptom Severity

This section delves into the internal consistency and reliability of the PCL-5 scores. It also examines associations between symptom cluster scores and overall PCL-5 score, considering potential biases.

## Cronbach's $\alpha$

The internal consistency of the PCL-5 was assessed using Cronbach's alpha; an alpha of 0.70 and above is regarded as satisfactory (Nunnally, 1978). The Cronbach's alpha scores were acceptable to good ( $\alpha$  range=0.61–0.78) for the cluster subscales, and high ( $\alpha$ =0.85) for the total score. Full results are presented in Table 2. The results suggest a high level of reliability in measuring total, avoidance, NegCog, and hyperarousal posttraumatic stress symptoms. The alpha for intrusion suggests lower internal consistency/reliability among intrusion cluster symptoms in this sample. The PCL-5 cluster subscale mean scores were moderate, and the mean total score was 3.32.

Table 4. Reliability for the PCL-5.

	<i>n</i>	<i>M</i>	<i>SD</i>	Cronbach's $\alpha$
Intrusion	5	3.51	0.70	0.61
Avoidance	2	3.85	1.01	0.71
NegCog	7	3.20	1.04	0.78
Hyperarousal	6	3.15	0.65	0.74
Total PCL-5 score	20	3.32	0.63	0.85

*Intrusion = PCL-5 intrusions question score. Avoidance = PCL-5 avoidance questions score. NegCog = PCL-5 NegCog questions score. Hyperarousal = PCL-5 hyperarousal questions score. PCL-5 = PTSD Checklist for DSM-5.*

## Overall PCL-5 Score

Correlations between scores on the symptom cluster questions and total PCL-5 score are shown in Table 3. Given that NegCog and hyperarousal cluster questions make up 35% and 30% of all questions respectively, high correlations between these questions and total score are expected. Surprisingly, avoidance cluster questions, which only make up 10% of the total questions, have a strong significant positive correlation with total score ( $\rho = 0.76$ , adj.  $p < 0.01$ ). This supports the empirical trend seen in Figure 1, where the area under the curve for  $TPC_{Avo}$  is much larger than the other TPCs, suggesting a bias towards overall higher scores on the PCL-5 for individuals with greater avoidance cluster symptoms.

To control for this potential bias in PCL-5 scores (overall significantly higher scores when individuals had more severe avoidance cluster symptoms), TPC membership was used as a factor for all non-numerical analyses.

Table 5. Intercorrelations Among Total PCL-5 Score and Cluster Questions.

	1	2	3	4	5
1. Intrusion	—				
2. Avoidance	0.35	—			
3. NegCog	0.17	0.65*	—		
4. Hyperarousal	0.34	0.56.	0.64*	—	
5. PCL-5 score	0.48.	0.76**	0.91***	0.84***	—

*Intrusion = Intrusion cluster questions score. Avoidance = Avoidance cluster questions score. NegCog = NegCog cluster questions score. Hyperarousal = Hyperarousal cluster questions score. Total PCL-5 Score = Total score on the PTSD Checklist for DSM-5. Intercorrelations calculated with Spearman's method, p-values have been corrected for multiple comparisons using FDR. Significance of  $p < 0.001 = \text{“****”}$ ,  $p < 0.01 = \text{“***”}$ ,  $p < 0.05 = \text{“*”}$ ,  $p < 0.10 = \text{“.”}$ .*

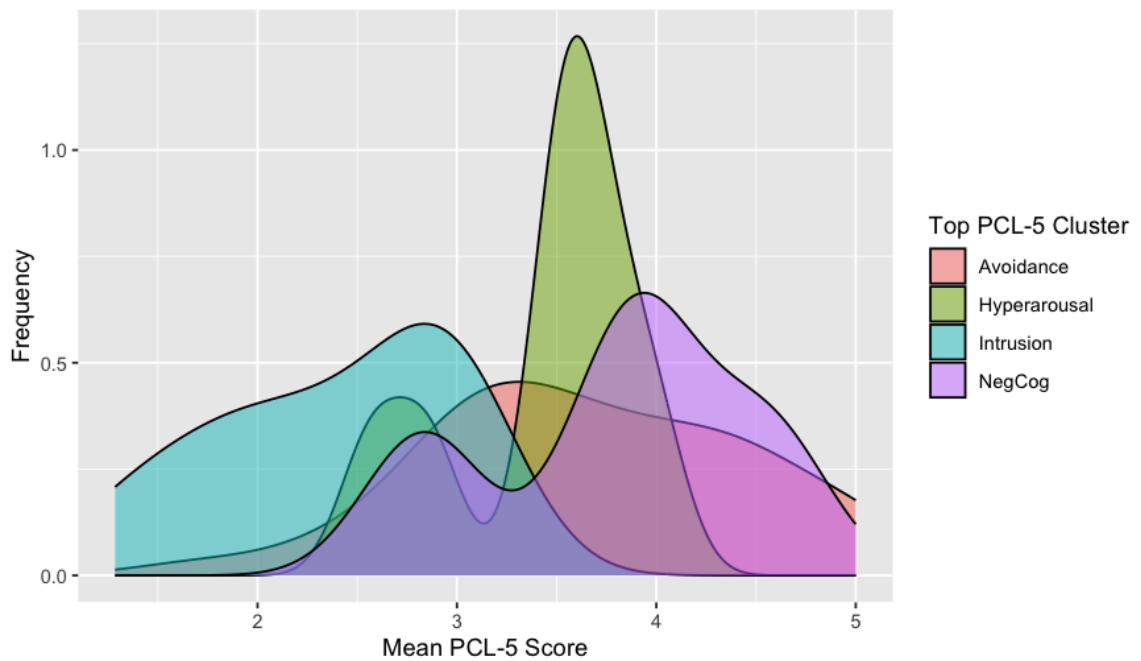


Figure 1. Mean PCL-5 Score by Highest Mean Cluster Subscale Score.

*A plot showing the difference in frequency of mean PCL-5 scores between participants who scored higher on symptom subscales (Avoidance, Hyperarousal, Intrusion, and NegCog). Mean PCL-5 score is shown on the X-axis, and frequency of responses at each mean PCL-5 score are shown on the Y-axis.*

### Main Analyses

The measures are divided into four categories and compared across symptom clusters. These include (1) sleep quality and continuity measures: TST, SE, #REM, SOL, ISI, and PSQI; measures of sleep architecture: N1%, N2%, N3%, REM%, REML, and WASO. (2) daytime and sleep measures of arousal: REMD, REM HRV, SCR negative, and SCR neutral. (3) spectral power sleep measures: frontal REM theta, beta, and gamma power. (4) self-report assessment measures: STAI-T, MEQ, and QIDS.

## Aim 1: Sleep Architecture, Quality, and Continuity Measures

While many of the sleep architecture, quality, and continuity measures demonstrated strong correlations with cluster question scores, only the negative correlation between TST and intrusion symptoms trended toward statistical significance ( $\rho = -0.67$ , *adj. p* < 0.10; see Tables 4, 5). Multiple pairwise comparisons between TPCs showed significant differences in these measures, including ISI, PSQI, and SOL (see Figure 2, Figure 3).

Hyperarousal symptoms had some of the lowest correlations with objective sleep quality and continuity measures, and the highest correlations with subjective measures (PSQI and ISI). Greater hyperarousal symptoms were non-significantly, weakly negatively associated with #REM ( $\rho = -0.17$ , *adj. p* = 0.92), and very weak to no association with TST ( $\rho = -0.10$ , *adj. p* > 0.05) and SE ( $\rho = 0.00$ , *adj. p* > 0.05). Hyperarousal symptoms were strongly positively correlated with ISI score ( $\rho = 0.55$ , *adj. p* > 0.05) and moderately positively correlated with PSQI score ( $\rho = 0.54$ , *adj. p* > 0.05).

Intrusion symptoms trended toward significance and showed a strong negative correlation with TST ( $\rho = -0.67$ , *adj. p* < 0.10). These symptoms also showed (non-significant) strong negative correlations with #REM ( $\rho = -0.48$ , *adj. p* > 0.05), a moderate negative association with SE ( $\rho = -0.49$ , *adj. p* > 0.05), and moderate to weak positive correlation with ISI ( $\rho = 0.30$ , *adj. p* > 0.05) and PSQI ( $\rho = 0.25$ , *adj. p* > 0.05).

NegCog symptoms demonstrated a non-significant, moderate negative correlation with SE ( $\rho = -0.30$ , *adj. p* > 0.05). They were also very weakly positively correlated with TST ( $\rho = 0.17$ , *adj. p* > 0.05), and very weakly positively correlated with PSQI ( $\rho = 0.32$ , *adj. p* > 0.05), ISI ( $\rho = 0.22$ , *adj. p* > 0.05).

Avoidance symptoms were non-significantly, weakly negatively associated with SE ( $\rho = -0.30$ ,  $\text{adj. } p > 0.05$ ), and moderately to weakly positively related to #REM ( $\rho = 0.14$ ,  $\text{adj. } p > 0.05$ ), ISI ( $\rho = 0.22$ ,  $\text{adj. } p > 0.05$ ), and PSQI ( $\rho = 0.32$ ,  $\text{adj. } p > 0.05$ ).

SOL was positively and most strongly correlated with NegCog symptoms ( $\rho = 0.49$ ,  $\text{adj. } p > 0.05$ ), avoidance symptoms ( $\rho = 0.41$ ,  $\text{adj. } p > 0.05$ ), and intrusion symptoms ( $\rho = 0.37$ ,  $\text{adj. } p > 0.05$ ). SOL was very weakly and non-significantly ( $\rho = 0.00$ ,  $\text{adj. } p > 0.05$ ) associated with hyperarousal symptoms.

Pairwise comparisons revealed that mean values of SOL were significantly ( $p < 0.05$ ) lower in the TPC<sub>Int</sub> group compared to the TPC<sub>Avo</sub> group. ISI ( $\text{adj. } p < 0.05$ ) and PSQI ( $\text{adj. } p < 0.01$ ) were significantly different between groups in pairwise comparisons (see Figure 2, Figure 3). None other pairwise differences between TPCs were significant for measures of sleep architecture, quality, and continuity (see Figure 2, Figure 3).



Table 6. Sleep Quality and Continuity Measures.

Variable	1	2	3	4	5	6	7	8	9
1. Intrusion	—								
2. Avoidance	0.35	—							
3. NegCog	0.17	0.65*	—						
4. Hyperarousal	0.34	0.56.	0.64*	—					
5. TST	-0.67.	0.06	-0.17	-0.10	—				
6. SE	-0.49	-0.26	-0.30	0.00	0.67.	—			
7. SOL	0.37	0.41	0.49	0.00	-0.49	-0.86**	—		
8. #REM	-0.48	-0.21	0.14	-0.23	0.13	0.02	0.08	—	
9. PSQI	0.25	0.28	0.32	0.54	-0.11	-0.23	0.37	-0.39	—
10. ISI	0.30	0.30	0.22	0.55	0.03	0.13	0.05	-0.37	0.77*

*Intrusion = Intrusion cluster questions score. Avoidance = Avoidance cluster questions score. NegCog = NegCog cluster questions score. Hyperarousal = Hyperarousal cluster questions score. TST = total sleep time. SE = sleep efficiency. SOL = sleep onset latency. #REM = number of REM periods. PSQI = Pittsburg Sleep Quality Index. ISI = Insomnia Severity Index. Intercorrelations calculated with Spearman's method, p-values have been corrected for multiple comparisons using FDR. Significance of  $p < 0.001 = \text{***}$ ,  $p < 0.01 = \text{**}$ ,  $p < 0.05 = \text{*}$ ,  $p < 0.10 = \text{.}$ .*

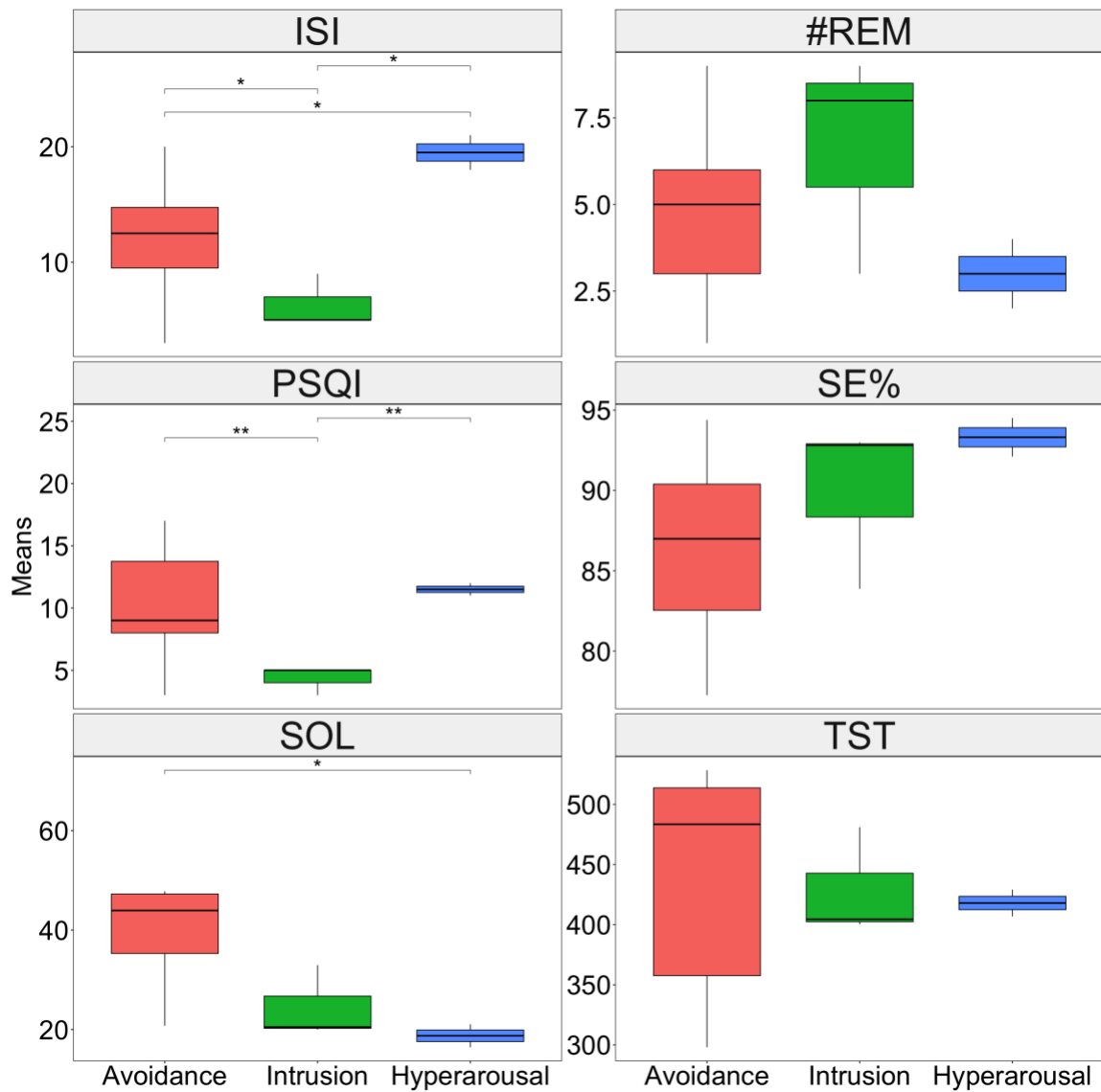


Figure 2. TPC Clusters and Sleep Quality and Continuity Measures.

*TPC<sub>Avo</sub>* shown in red, *TPC<sub>Int</sub>* shown in Green, *TPC<sub>Hyp</sub>* shown in blue. *TPC<sub>Neg</sub>* not shown due to missing data ( $n = 1$ ). Significance of  $p < 0.05$  is shown with one asterisk (\*), and  $p < 0.01$  is shown with two asterisks (\*\*). #REM = Number of REM periods during PSG night. SE = sleep efficiency. SOL = sleep onset latency.

Table 7. Sleep Architecture Measures.

Variable	1	2	3	4	5	6	7	8	9
1. Intrusion	—								
2. Avoidance	0.35	—							
3. NegCog	0.17	0.65*	—						
4. Hyperarousal	0.34	0.56.	0.64*	—					
5. N1%	-0.23	0.03	-0.04	0.10	—				
6. N2%	0.14	0.37	-0.19	0.10	0.27	—			
7. N3%	-0.15	-0.20	-0.04	-0.24	-0.41	-0.37	—		
8. REML	-0.24	-0.13	-0.27	-0.41	0.51	0.10	-0.01	—	
9. WASO	-0.19	-0.38	-0.16	-0.41	0.40	-0.33	-0.11	0.55	—

*Intrusion = intrusion cluster questions score. Avoidance = avoidance cluster questions score. NegCog = NegCog cluster questions score. Hyperarousal = hyperarousal cluster questions score. N1% = percent of sleep that was NREM1. N2% = percent of sleep that was NREM2. N3% = percent of sleep that was NREM3. REML = REM Latency. WASO = wake after sleep onset. Intercorrelations calculated with Spearman's method, p-values have been corrected for multiple comparisons using FDR. Significance of  $p < 0.001 = \text{“***”}$ ,  $p < 0.01 = \text{“**”}$ ,  $p < 0.05 = \text{“*”}$ ,  $p < 0.10 = \text{“.”}$*

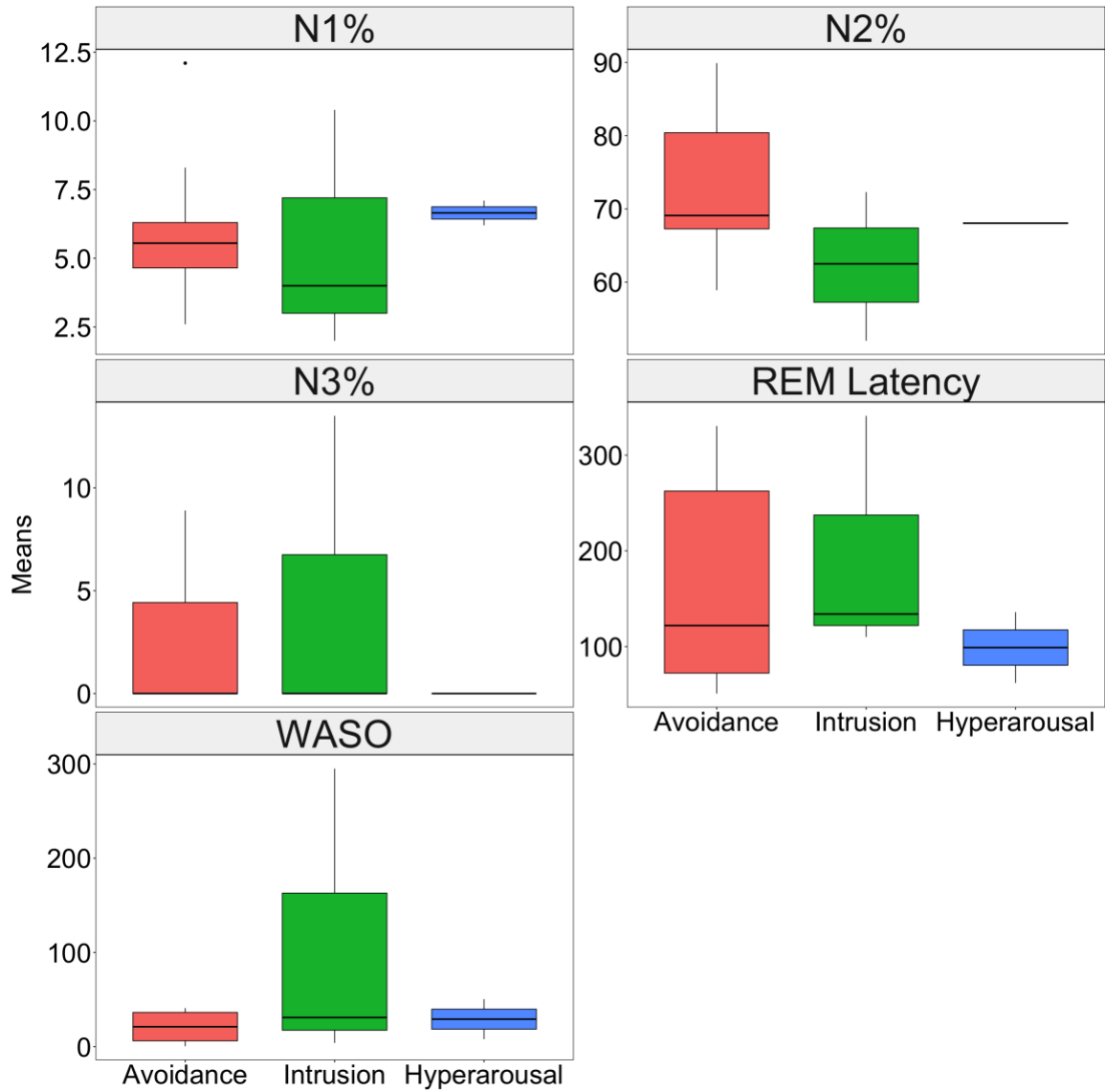


Figure 3. TPC Clusters and Sleep Architecture Measures.

*TPC<sub>Avo</sub>* shown in red, *TPC<sub>Int</sub>* shown in Green, *TPC<sub>Hyp</sub>* shown in blue. *TPC<sub>Neg</sub>* not shown due to missing data ( $n = 1$ ). *N1%* = percent of sleep that was NREM1. *N2%* = percent of sleep that was NREM2. *N3%* = percent of sleep that was NREM3. *REML* = REM Latency. *WASO* = wake after sleep onset.

## Aim 2: Daytime and Sleep Measures of Arousal

None of the correlations between daytime and sleep measures of arousal and cluster symptoms reached statistical significance (see Table 6). Pairwise comparisons between TPCs and these measures also didn't reach statistical significance (see Figure 4).

All symptom clusters had a positive, non-significant correlation with REMD. NegCog symptoms had the strongest positive correlation with REMD ( $\rho = 0.32$ , *adj. p* > 0.05), followed by hyperarousal symptoms ( $\rho = 0.18$ , *adj. p* > 0.05). REMD showed weak positive correlations with avoidance ( $\rho = 0.19$ , *adj. p* > 0.05) and intrusion ( $\rho = 0.01$ , *adj. p* > 0.05) symptoms.

All symptom clusters had a negative, non-significant correlation with REM HRV. REM HRV was most strongly correlated with intrusion ( $\rho = -0.22$ , *adj. p* > 0.05) and avoidance ( $\rho = -0.17$ , *adj. p* > 0.05) symptoms. It was weakly associated with hyperarousal ( $\rho = -0.10$ , *adj. p* > 0.05) and negligibly associated with NegCog ( $\rho = -0.01$ , *adj. p* > 0.05) symptoms.

Hyperarousal symptoms were (non-significantly) most strongly negatively correlated with both SCR negative ( $\rho = -0.47$ , *adj. p* > 0.05) and SCR neutral ( $\rho = -0.47$ , *adj. p* > 0.05). NegCog symptoms were negatively, strongly correlated with SCR negative ( $\rho = -0.23$ , *adj. p* > 0.05), but were only very weakly negatively correlated with SCR neutral ( $\rho = -0.10$ , *adj. p* > 0.05). Intrusion symptoms had a weak positive correlation with SCR neutral ( $\rho = 0.12$ , *adj. p* > 0.05). SCR neutral and SCR negative were weakly negatively associated with avoidance symptoms ( $\rho = 0.12$ , *adj. p* > 0.05;  $\rho = 0.12$ , *adj. p* > 0.05).

Table 8. Daytime and Sleep Measures of Arousal.

Variable	1	2	3	4	5	6	7	8
1. Intrusion	—							
2. Avoidance	0.35	—						
3. NegCog	0.17	0.65*	—					
4. Hyperarousal	0.34	0.56.	0.64*	—				
5. REMD	0.01	0.19	0.32	0.18	—			
6. REM HRV	-0.22	-0.17	-0.01	-0.10	-0.26	—		
7. SCR neu	0.12	-0.17	-0.10	-0.47	-0.01	0.28	—	
8. SCR neg	-0.04	-0.14	-0.23	-0.47	0.01	0.52	0.73*	—

*Intrusion = intrusion cluster questions score. Avoidance = avoidance cluster questions score. NegCog = NegCog cluster questions score. Hyperarousal = hyperarousal cluster questions score. REMD = REM density. REM HRV = heart rate variability during REM measured by RMSSD. SCR neu = change in skin conductance response from baseline to neutral SDI. SCR neg = change in skin conductance response from baseline to nightmare/trauma SDI. Intercorrelations calculated with Spearman's method, p-values have been corrected for multiple comparisons using FDR. Significance of  $p < 0.001 = \text{"***"} , p < 0.01 = \text{"**"} , p < 0.05 = \text{"*"} , p < 0.10 = \text{"."} .$*

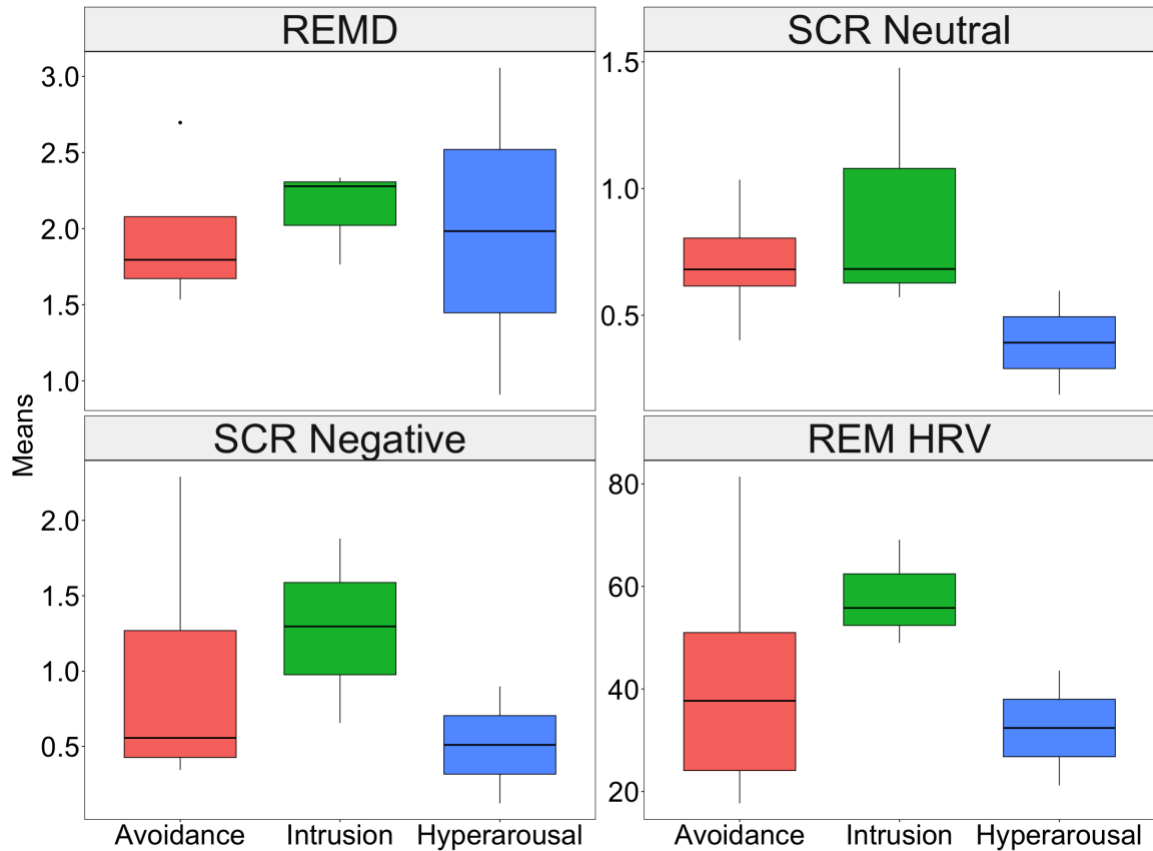


Figure 4. TPC Clusters and Daytime and Sleep Measures of Arousal.

*TPC<sub>Avo</sub> shown in red, TPC<sub>Int</sub> shown in Green, TPC<sub>Hyp</sub> shown in blue. TPC<sub>Neg</sub> not shown due to missing data (n = 1). No significant group differences. REMD = REM density during PSG night. REM HRV = RMSSD (root mean square of successive differences between RR intervals). SCR negative = skin conductance response during nightmare or trauma SDI. SCR neutral = skin conductance response during neutral SDI. SE = sleep efficiency.*

### Aim 3: Spectral Power Sleep Measures

Statistical analyses revealed no significant correlations between daytime and sleep measures of arousal and PCL-5 cluster symptom scores after correcting for multiple comparisons (see Table 7). Only NegCog symptoms trended towards significance in association with frontal REM theta power, but the correlation was very weak ( $\rho = 0.05$ ,

adj.  $p = 0.10$ ). Pairwise comparisons between TPCs and these measures did not yield any statistically significant results (see Figure 5).

Hyperarousal symptoms were non-significantly, most strongly negatively correlated with frontal REM theta power ( $\rho = -0.35$ , adj.  $p > 0.05$ ) across all symptom clusters. Intrusion symptoms were very weakly negatively correlated with frontal REM theta power ( $\rho = -0.02$ , adj.  $p > 0.05$ ). Avoidance scores had the highest positive correlation with frontal REM theta power ( $\rho = 0.25$ , adj.  $p > 0.05$ ). NegCog symptoms trended towards significance and were weakly positively correlated with frontal REM theta power ( $\rho = 0.05$ , adj.  $p = 0.10$ ).

None of the correlations with frontal REM gamma power reached statistical significance, and it had the strongest positive association with avoidance symptoms ( $\rho = 0.31$ , adj.  $p > 0.05$ ; see Table 7). Intrusion symptoms had a weak positive association with frontal REM gamma power ( $\rho = 0.19$ , adj.  $p = 0.10$ ), while the association was weak and negligible with negative ( $\rho = 0.10$ , adj.  $p > 0.05$ ). and hyperarousal symptoms ( $\rho = 0.07$ , adj.  $p > 0.05$ ).

As with gamma and theta, none of the associations with frontal REM beta power reached statistical significance. Hyperarousal symptoms were most strongly and negatively associated with frontal REM beta power ( $\rho = -0.44$ , adj.  $p > 0.05$ ), followed by intrusion symptoms ( $\rho = -0.36$ , adj.  $p > 0.05$ ). Avoidance and NegCog symptoms were negligibly associated with it, although in opposite directions ( $\rho = 0.01$ , adj.  $p > 0.05$ ;  $\rho = -0.01$ , adj.  $p > 0.05$ ; see Table 7).

Pairwise comparisons of measures of the spectral power measures found no significant group differences between TPCs (see Figure 5).



Table 9. Spectral Power Sleep Measures.

Variables	1	2	3	4	5	6	7
1. Intrusion	—						
2. Avoidance	0.35	—					
3. NegCog	0.17	0.65*	—				
4. Hyperarousal	0.34	0.56.	0.64*	—			
5. Gamma	0.19	0.31	0.10	0.07	—		
6. Beta	-0.36	0.01	-0.01	-0.44	0.68	—	
7. Theta	-0.02	0.24	0.05	-0.35	0.50	0.47	—

*Intrusion = intrusion cluster questions score. Avoidance = avoidance cluster questions score. NegCog = NegCog cluster questions score. Hyperarousal = hyperarousal cluster questions score. Gamma = EEG-measured frontal region brain activity during REM in the gamma band range [~ 30 to 100 Hz]. Beta = EEG-measured frontal region brain activity during REM in the beta band range [~13–30 Hz]. Theta = EEG-measured frontal region brain activity during REM in the theta band range [~ 4 to 8 Hz]. Intercorrelations calculated with Spearman’s method, p-values have been corrected for multiple comparisons using FDR. Significance of  $p < 0.001 = “***”$ ,  $p < 0.01 = “**”$ ,  $p < 0.05 = “*”$ ,  $p < 0.10 = “.”$ .*

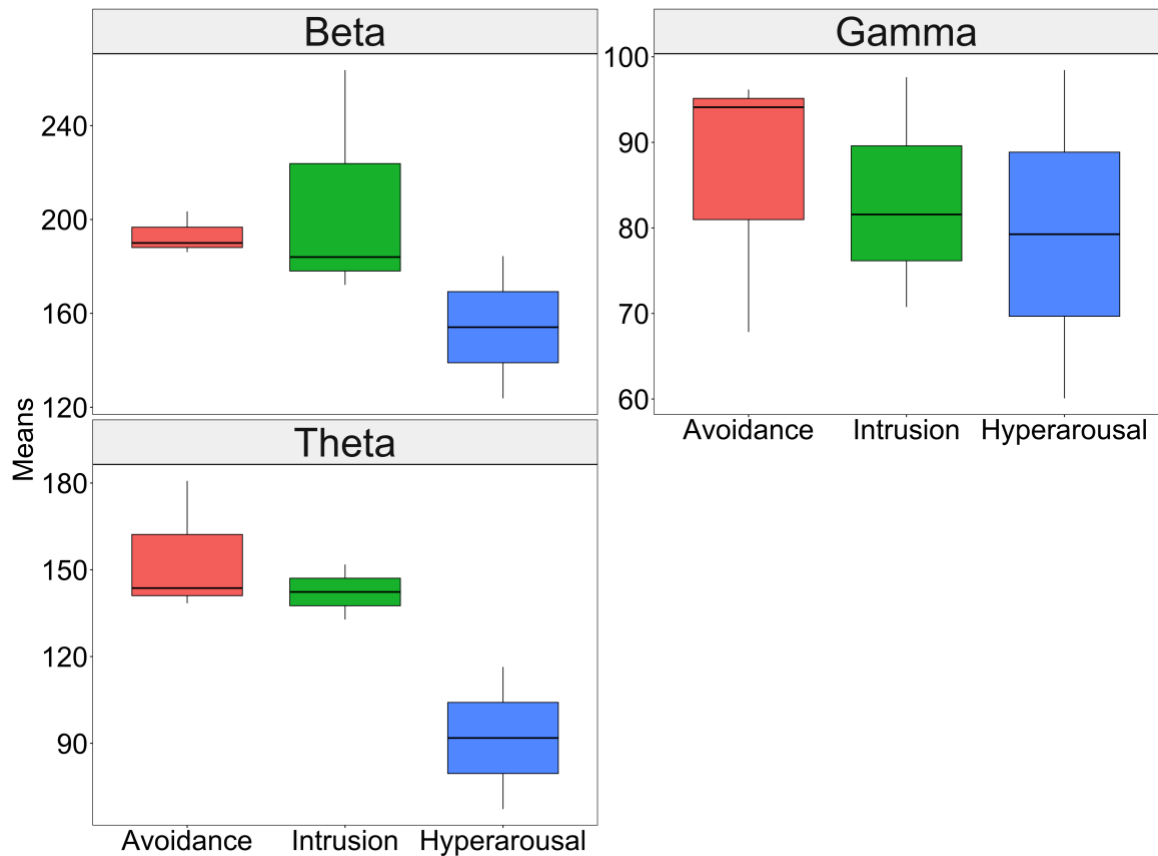


Figure 5. TPC Clusters and Spectral Power Sleep Measures.

*TPC<sub>Avo</sub> shown in red, TPC<sub>Int</sub> shown in Green, TPC<sub>Hyp</sub> shown in blue. TPC<sub>Neg</sub> not shown due to missing data ( $n = 1$ ). Gamma = EEG-measured frontal region brain activity during REM in the gamma band range [ $\sim 30$  to  $100$  Hz]. Beta = EEG-measured frontal region brain activity during REM in the beta band range [ $\sim 13$ – $30$  Hz]. Theta = EEG-measured frontal region brain activity during REM in the theta band range [ $\sim 4$  to  $8$  Hz].*

#### Aim 4: Self-Report Assessment Measures

Spearman's rank correlation coefficient showed a strong positive, statistically significant correlation between hyperarousal symptoms and QIDS score ( $\rho = 0.73$ , *adj. p* < 0.05), and a moderate correlation with STAI-T score that trended towards significance

( $\rho = 0.54$ , *adj. p* < 0.10; see Table 8). No other correlations or any of the TPC pairwise comparisons achieved statistical significance (see Figure 6).

Intrusion symptoms were positively, weakly associated with QIDS ( $\rho = 0.33$ , *adj. p* > 0.05), and negatively, very weakly associated with MEQ ( $\rho = -0.15$ , *adj. p* > 0.05), and very weakly positively associated with STAI-T ( $\rho = 0.14$ , *adj. p* > 0.05).

NegCog symptoms were positively, moderately associated with STAI-T score ( $\rho = 0.42$ , *adj. p* > 0.05), and weakly with QIDS ( $\rho = 0.39$ , *adj. p* > 0.05). MEQ scores were negatively, weakly associated with NegCog symptoms ( $\rho = -0.26$ , *adj. p* > 0.05).

Avoidance symptoms were positively, moderately correlated with QIDS ( $\rho = 0.24$ , *adj. p* > 0.05), and very weakly, positively correlated with STAI-T ( $\rho = 0.14$ , *adj. p* > 0.05) and negatively with MEQ ( $\rho = 0.15$ , *adj. p* > 0.05; see Table 8)

Table 10. Self-Report Assessment Measures.

Variables	1	2	3	4	5	6	7
1. Intrusion	—						
2. Avoidance	0.35	—					
3. NegCog	0.17	0.65*	—				
4. Hyperarousal	0.34	0.56.	0.64*	—			
5. MEQ	-0.15	-0.15	-0.26	-0.27	—		
6. QIDS	0.33	0.24	0.39	0.73*	-0.48	—	
7. STAI-T	0.14	0.10	0.42	0.54.	-0.64*	0.84**	—

*Intrusion = intrusion cluster questions score. Avoidance = avoidance cluster questions score. NegCog = NegCog cluster questions score. Hyperarousal = hyperarousal cluster questions score. MEQ = Morningness-Eveningness Questionnaire. QIDS = Quick Inventory of Depressive Symptomatology. STAI-T = Spielberg's State-Trait Anxiety Inventory. Intercorrelations calculated with Spearman's method, p-values have been corrected for multiple comparisons using FDR. Significance of  $p < 0.001 = \text{****}$ ,  $p < 0.01 = \text{***}$ ,  $p < 0.05 = \text{*}$ ,  $p < 0.10 = \text{.}$ .*

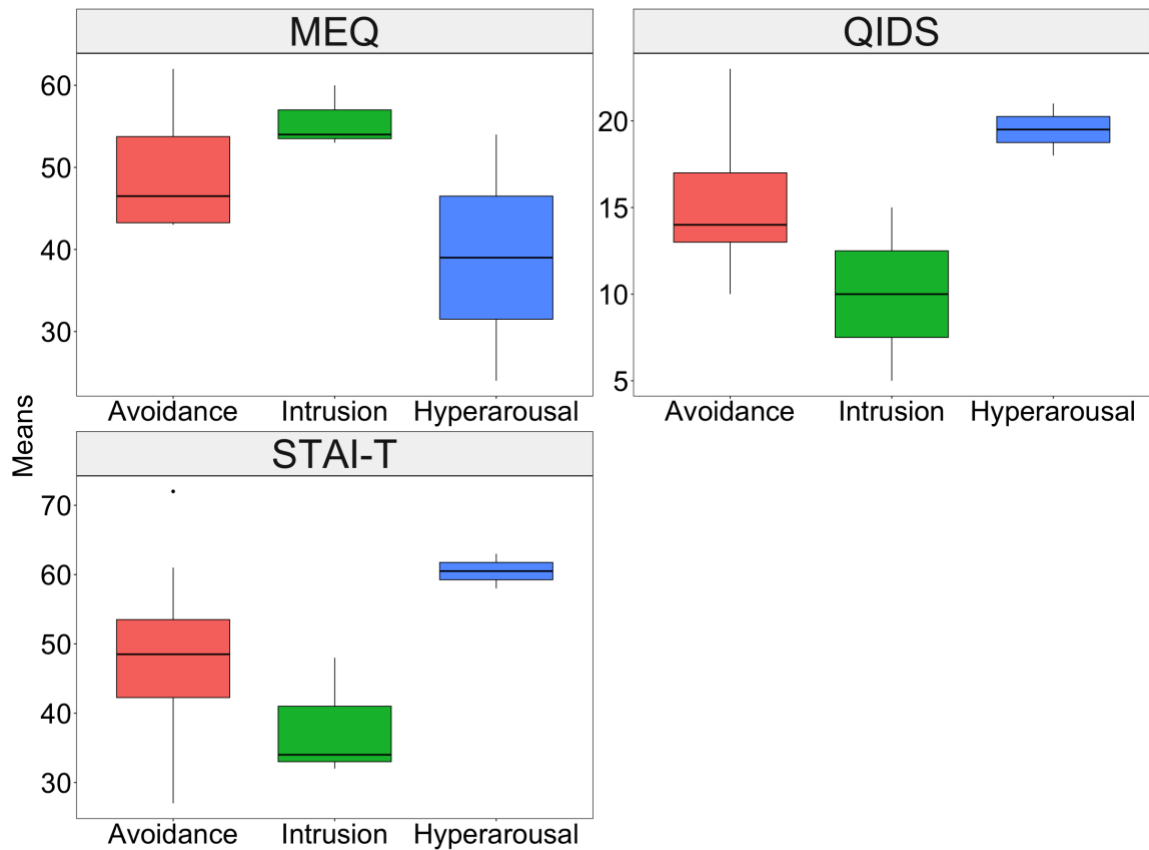


Figure 6. TPC Clusters and Self-Report Assessment Measures.

*TPCAvo* shown in red, *TPCInt* shown in Green, *TPCHyp* shown in blue. *TPCNeg* not shown due to missing data ( $n = 1$ ). *MEQ* = Morningness-Eveningness Questionnaire. *QIDS* = Quick Inventory of Depressive Symptomatology. *STAI-T* = Spielberger State Anxiety Inventory. *ISI* = Insomnia Severity Index. *PSQI* = Pittsburg Sleep Quality Index.

Empirically, as shown in Figure 7, the mean REM HRV values for each cluster are significantly inversely correlated with STAI-T scores, positively correlated with MEQ scores, and moderately, negatively correlated with QIDS scores. REM HRV scores appear to inversely correlate with REMD scores (Figure 8); mean REMD across TPC groups is strongly positively correlated with STAI-T, strongly negatively correlated with MEQ, and moderately, positively correlated with QIDS scores.

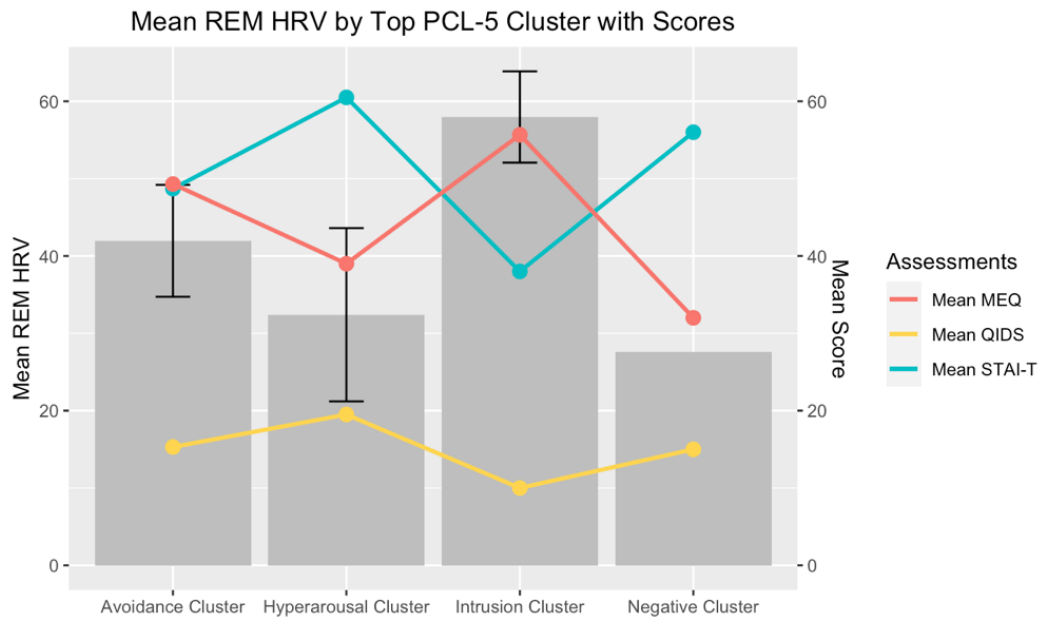


Figure 7. TPC, REM HRV, and Mental Health and Circadian Assessments.

*Mean REM HRV shown on Y-axis with overlay of mean MEQ, QIDS, and STAI-T scores. Top PCL-5 Cluster shown on X-axis. MEQ = Morningness-Eveningness Questionnaire, shown in red. QIDS = Quick Inventory of Depressive Symptomatology, shown in yellow. STAI-T = Spielberger State Anxiety Inventory, shown in blue.*

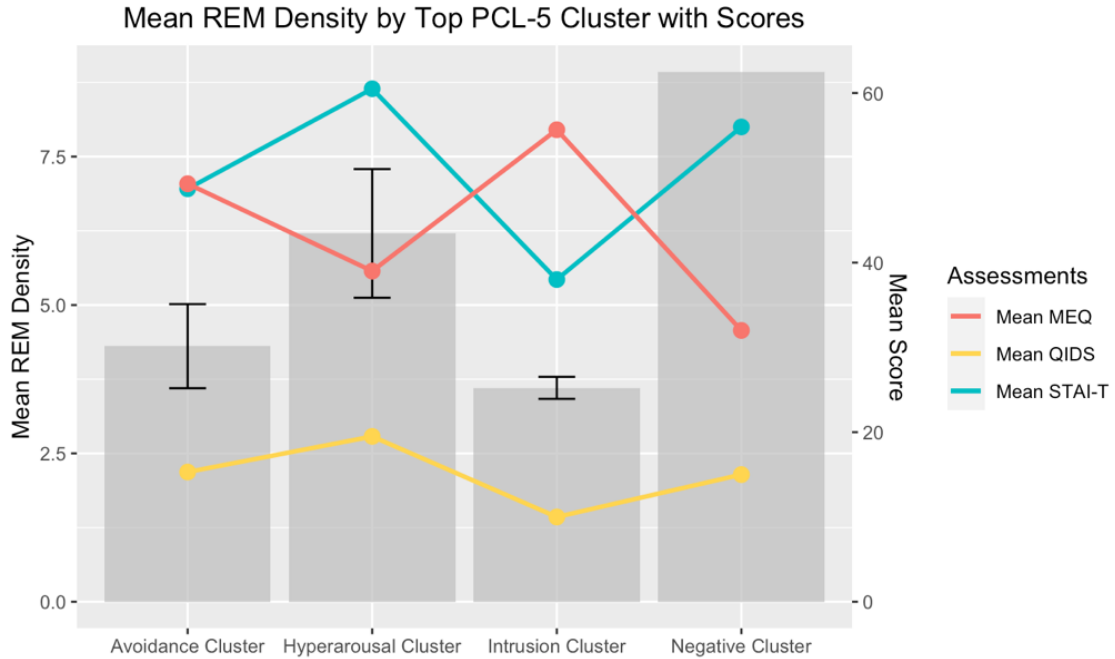


Figure 8. TPC, REMD, and Mental Health and Circadian Assessments.

*Mean REMD shown on Y axis with overlay of mean MEQ, QIDS, and STAI-T scores. Top PCL-5 Cluster shown on X-axis. MEQ = Morningness-Eveningness Questionnaire, shown in red. QIDS = Quick Inventory of Depressive Symptomatology, shown in yellow. STAI-T = Spielberger State Anxiety Inventory, shown in blue.*

### Exploratory Analysis #1

SVM classification accuracy of the MDS physiological measures configuration was 72.72%, indicating a substantial degree of correspondence between the MDS-derived clusters and the ground truth facet coding TPCs (see Figure 9).

When applying the SVM classifier to the subjective MDS configuration data, it exhibited a fair classification accuracy of 62%, as shown in Figure 10.

## MDS-SVM Configuration Plot

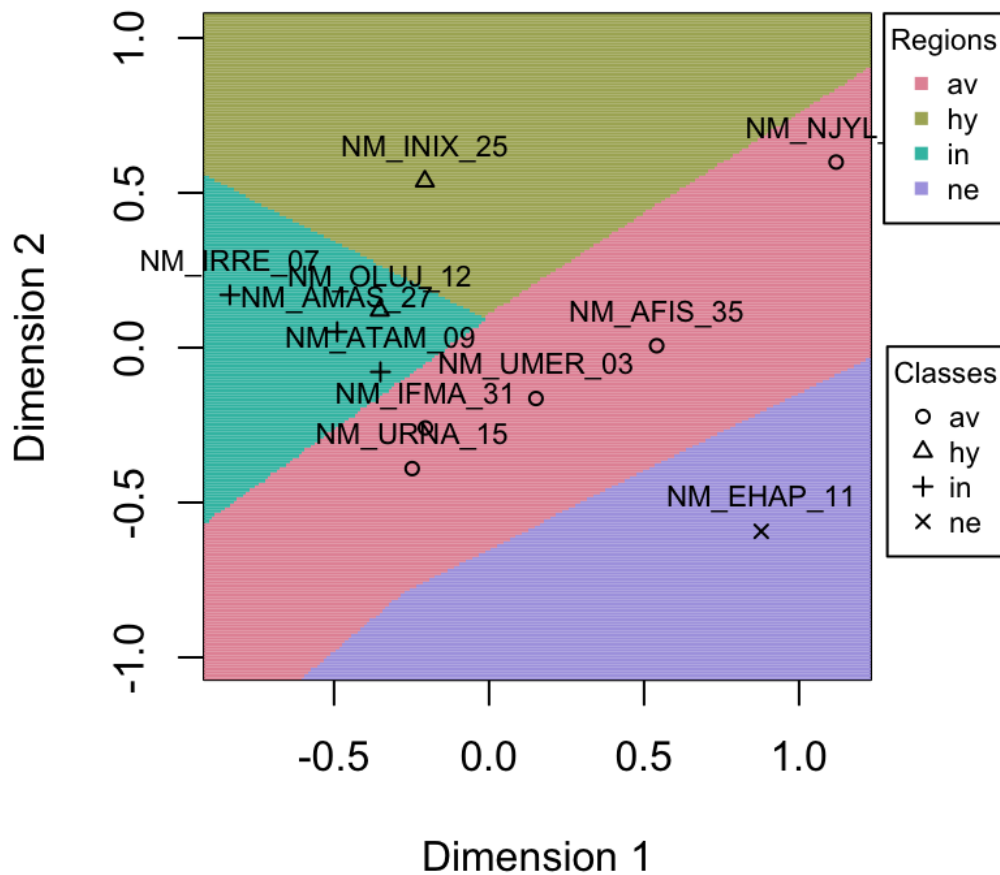


Figure 9. MDS-SVM Configuration with Physiological Measures.

*MDS configuration of predicted versus groundtruth Top PCL-5 Clusters based on physiological measures. av = Avoidance cluster. hy = Hyperarousal cluster. in = Intrusion Cluster. ne = NegCog cluster. Regions are based on groundtruth facet coding and classes are the SVM predicted classes.*



## MDS-SVM Configuration Plot

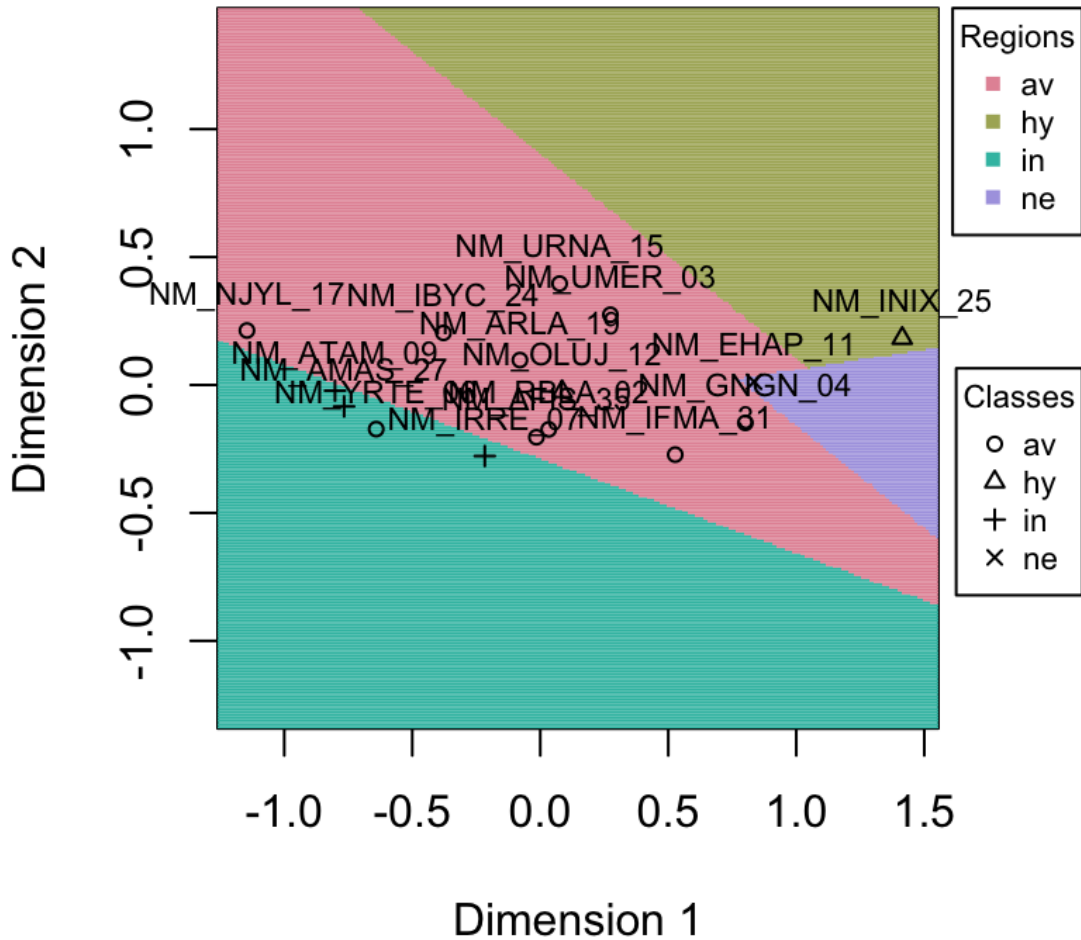


Figure 10. MDS-SVM Configuration with Subjective Measures.

*MDS configuration of predicted versus groundtruth Top PCL-5 Clusters based on subjective measures. av = Avoidance cluster. hy = Hyperarousal cluster. in = Intrusion Cluster. ne = NegCog cluster. Regions are based on groundtruth facet coding and classes are the SVM predicted classes.*

## Exploratory Analysis #2

A two-way ANOVA was used to examine the impact of the variable Theta on the REMD values, controlling for Number of REM Periods. The analysis revealed a statistically significant effect of Theta on REMD ( $F(1, 40) = 11.78, p < 0.01$ ), indicating that different levels of Theta are associated with significant differences in REMD values, as shown in Figure 11.

In another two-way ANOVA investigating the influence of frontal REM gamma power on REMD, controlling for #REM. The main effect of frontal REM gamma power was not significant ( $F(1, 39) = 0.119, p = 0.7323$ ). However, a significant main effect emerged for #REM ( $F(1, 39) = 4.605, p = 0.0382$ ), suggesting that varying numbers of REM Periods are significantly associated with distinct REMD values, as shown in Figure 12. Additionally, the interaction effect between frontal REM gamma power and #REM approached significance ( $F(1, 39) = 3.117, p = 0.09$ ), indicating that the combined effect of frontal REM gamma power and #REM may have a nuanced impact on REMD.

In a linear regression model investigating the relationship between REMD and #REM, the intercept was found to be statistically significant ( $b = 9.341, SE = 2.544, t(36) = 3.671, p < 0.01$ ); this indicates that the mean estimated value of REMD is significantly different from zero when #REM is at baseline (REM periods 1 and 2).

Among the categorical predictors, REM periods 8 ( $b = -5.57, SE = 2.72, t(36) = -2.05, p < 0.05$ ) and 9 ( $b = -6.04, SE = 2.62, t(36) = -2.30, p = 0.03$ ) were found to be statistically significant. This suggests that these REM periods tend to have significantly different REMD compared to baseline, with REM period 8 showing a 5.57 decrease in REMD, and 6.04 lower REMD in REM period 9.

REM periods 3-6 did not reach conventional levels of statistical significance ( $p > .05$ ). However, there is a trend suggesting potential associations among two of the REM periods; there was a marginally significant negative trend with REM period 3 ( $b = -5.75$ ,  $SE = 2.85$ ,  $t(36) = -1.895$ ,  $p = 0.05$ ) and REM period 4 ( $b = -5.21$ ,  $SE = 2.75$ ,  $t(36) = -1.895$ ,  $p = 0.07$ ). Empirically, an upward trend in REMD from the two previous periods is seen across all groups, regardless of #REM (see Figure 11, Figure 12).

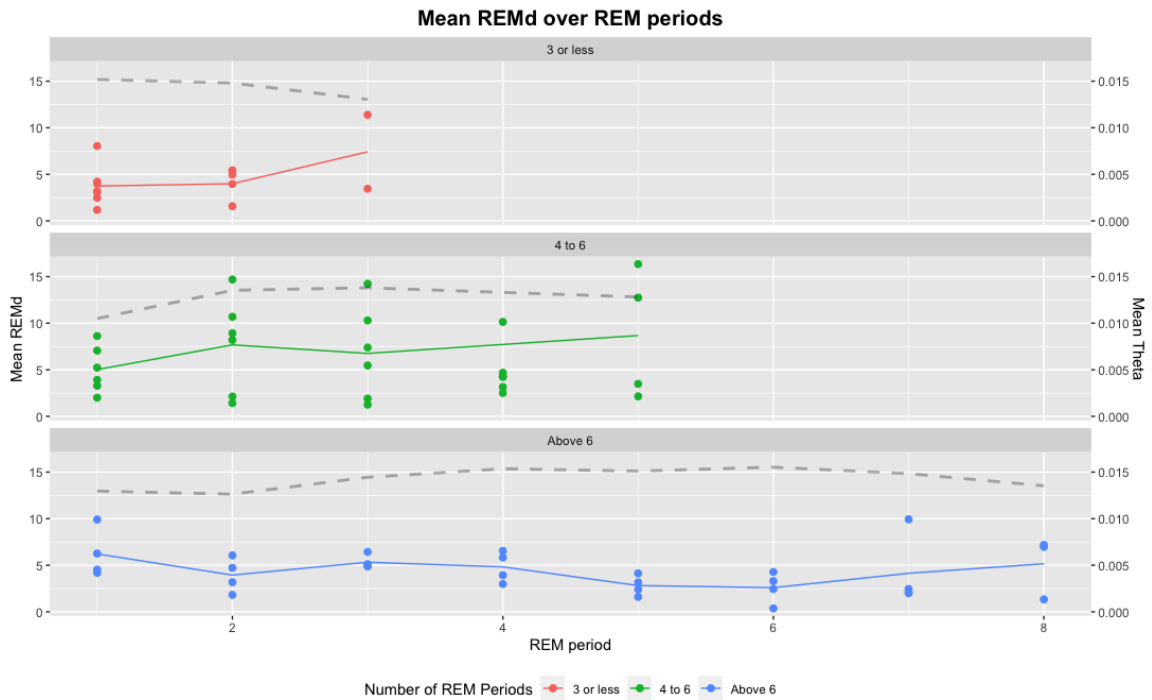


Figure 11. Mean REMD over REM Periods and Theta.

*Number of REM Period shown on the X-axis, Mean REMD shown on left Y-axis, and Mean Theta shown on right Y-axis. Participants with three or less REM periods during the PSG night are shown in the top plot in red, participants with 4 to 6 REM periods are shown in green, and participants with greater than 6 REM periods are shown in blue. Dots represent participants. Mean Theta is plotted as a gray dotted line.*

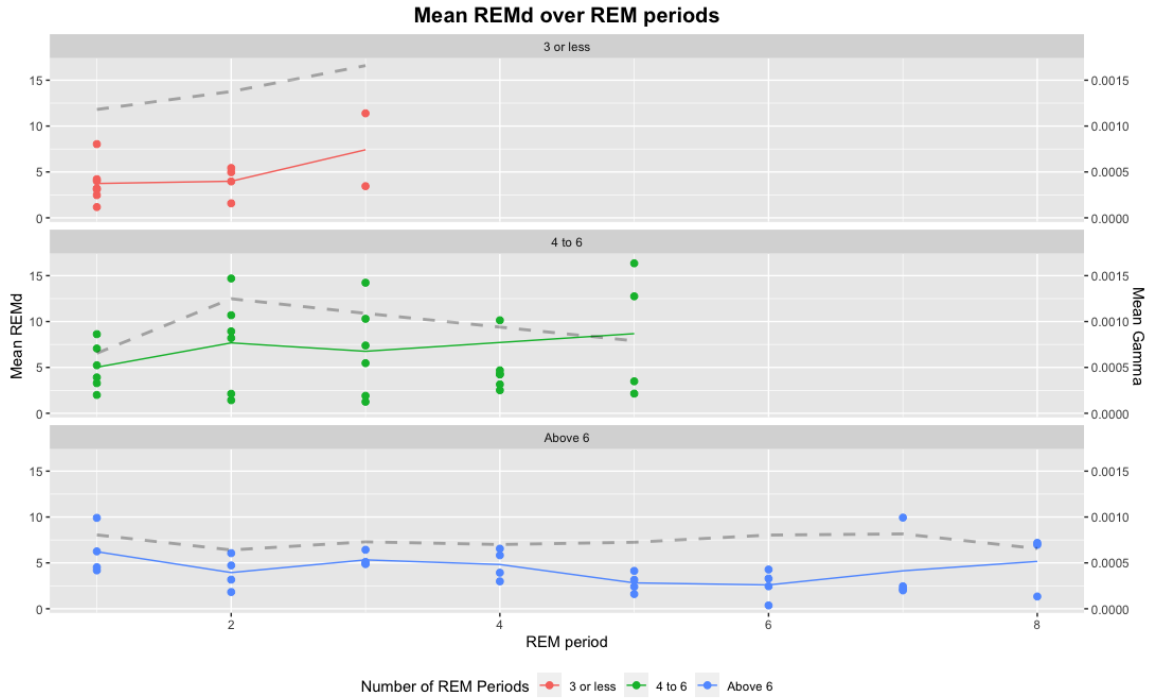


Figure 12. Mean REMD Over REM Periods and Gamma.

*Number of REM Period shown on the X-axis, Mean REMD shown on left Y-axis, and Mean Gamma shown on right Y-axis. Participants with three or less REM periods during the PSG night are shown in red, participants with 4 to 6 REM periods are shown in green, and participants with greater than 6 REM periods are shown in blue. Dots represent participants. Mean Gamma is plotted as a gray dotted line.*

## Chapter IV.

### Discussion

Likely owing in part to the small sample size, few relationships in the correlational analyses or pairwise comparisons reached statistical significance (see Appendix 1 for full correlational network). Several noteworthy trends did emerge between symptom clusters/TPC (Top PCL-5 Cluster) membership and the measures.

One key finding is that hyperarousal symptoms have some of the lowest associations with physiological measures of sleep quality and continuity, yet the strongest positive associations with subjective measures of sleep quality, ISI and PSQI (see Table 6). Meanwhile, intrusion symptoms displayed a strong negative correlation with TST, which trended towards significance. Pairwise comparisons between TPCs revealed several significant group differences (see Figure 2). SOL was significantly higher in TPC<sub>Av0</sub> compared to TPC<sub>Hyp</sub>. Consistent with the correlational analyses, TPC<sub>Hyp</sub> had significantly higher ISI and PSQI scores compared to TPC<sub>Int</sub> and TPC<sub>Av0</sub>. Surprisingly, TPC<sub>Av0</sub> also had significantly higher ISI scores compared to TPC<sub>Int</sub>. Potential interpretations are discussed in “Hypothesis 1: Sleep Architecture, Quality, and Continuity Measures” below.

Another key finding is the negative correlation between all symptom clusters and HRV during REM sleep, and their positive correlation with REMD (see Table 8). REMD was most strongly associated with NegCog, hyperarousal, and avoidance symptoms, while REM HRV was most strongly associated with intrusion and avoidance symptoms. These relationships appear to correspond to empirically identified inverse correlations between REMD and REM HRV measures and STAI-T and QIDS scores (see Figure 7,

Figure 8). Higher mean REMD in TPC<sub>Hyp</sub>, TPC<sub>Av0</sub>, and TPC<sub>Neg</sub> corresponded to equivalently higher STAI-T and QIDS scores, while higher mean REM HRV in TPC<sub>Int</sub> and TPC<sub>Av0</sub> correspond with lower STAI-T and QIDS scores (see Figure 7, Figure 8). These findings may suggest that REMD and REM HRV measure different kinds of arousal during sleep.

Lastly, a weak, positive correlation between NegCog symptoms and frontal REM theta power trended towards significance (see Table 9). This finding may point towards less disrupted emotional memory processing during REM in individuals with greater NegCog symptoms. Potential interpretations regarding spectral power analyses are discussed in the “Hypothesis 3: Spectral Power Sleep Measures” section below.

#### Hypothesis 1: Sleep Architecture, Quality, and Continuity Measures

It was hypothesized that more severe hyperarousal and to a lesser extent intrusion symptoms would be negatively associated with measures of objective and subjective sleep quality and continuity. Weaker correlations between NegCog and avoidance cluster symptoms and these measures were predicted.

As expected, TPC<sub>Av0</sub> and TPC<sub>Int</sub> had significantly lower mean scores on the ISI assessment compared to TPC<sub>Hyp</sub>, suggesting less subjective insomnia-related symptoms and symptom-related daytime distress. Surprisingly, TPC<sub>Av0</sub> also demonstrated significantly higher mean ISI scores compared to TPC<sub>Int</sub>. TPC<sub>Hyp</sub>, and contrary to our hypotheses, TPC<sub>Av0</sub> had significantly higher scores on the PSQI compared to TPC<sub>Int</sub>, representing poorer subjective sleep maintenance and quality in these clusters. The hyperarousal symptom findings are consistent with literature showing greater subjective sleep disruption (higher PSQI scores) in individuals with greater hyperarousal symptom

severity (Van Wyk et al., 2016). However, to our knowledge these findings are the first to show higher subjective sleep disturbance in individuals with higher avoidance scores. Our results indicate that higher scores on hyperarousal cluster symptoms correspond to increased reporting of subjective sleep disturbances and distress related to sleep symptoms — and add that individuals with greater avoidance symptoms may also experience similar difficulties.

The results concerning objective sleep measures did not consistently align with our initial hypotheses. Intrusion and NegCog symptoms showed the strongest correlations with objective measures of sleep quality, while hyperarousal symptoms were only weakly associated with objective sleep measures. Hyperarousal symptoms were (non-significantly) strongly negatively correlated with REM latency (REML), moderately negatively correlated with WASO, and strongly positively correlated with N1, and had only weak correlations with all other measures. Pairwise comparisons supported these findings; TPC<sub>Hyp</sub> had non-significantly lower REML, higher SE, a greater amount of N1 sleep, a negligible amount of N3 sleep, and a moderate amount of WASO. These findings are mostly contrary to existing literature, which has shown that hyperarousal symptom severity is correlated with an increase in WASO, REML and SOL, and a decrease in SE and TST (Babson et al., 2011; Brownlow et al., 2022; Mellman et al., 1995; Van Wyk et al., 2016). However, the results are consistent with correlations seen between hyperarousal symptom severity and sleep architecture variables, namely greater N1 and N2 sleep (Brownlow et al., 2022). The inconsistencies in the objective sleep measures may be due to the small sample size, and future research leveraging a dimensional

approach may help uncover more accurate relationships between these measures and symptom clusters.

Contrary to our expectation, SOL was significantly higher in TPC<sub>AvO</sub> compared to TPC<sub>Hyp</sub>. The correlational analyses showed strong, non-significant positive relationships between both avoidance and NegCog symptoms and SOL. This finding is in line with literature indicating avoidance symptoms are related to difficulty both initiating and maintaining sleep (Babson et al., 2011). Two proposed underlying mechanisms are (1) that PTSD-related avoidance of negative thoughts paradoxically leads to increased arousal that interferes with sleep onset (Babson et al., 2011), and (2) that avoidance behaviors may extend to the avoidance of sleep due to anxieties related to TRNs (trauma-related nightmares) (Uhde et al., 2000 as cited in Babson et al., 2011). The inclusion criteria for the study included frequent TRNs, which may substantiate that individuals in this study with avoidance-related symptoms were avoiding sleep due to anxiety associated with experiencing TRNs. The additional finding of a strong association between SOL and NegCog symptoms, although non-significant, might bolster the notion that negative thoughts could contribute to heightened pre-sleep arousal, thus impeding the ability to initiate sleep.

REM Latency (REML) is not consistently abnormal in individuals with PTSD, but it is considered to be a measure of REM pressure in depression (Kobayashi et al., 2007; Palagini et al., 2013; Zhang et al., 2019). Although non-significant, it is notable that TPC<sub>Hyp</sub> had the lowest mean REML while also demonstrating the highest mean QIDS score. TPC<sub>Int</sub> had the highest mean REML and lowest mean QIDS score, while the mean REML and mean QIDS score of the TPC<sub>AvO</sub> fell between those of TPC<sub>Hyp</sub> and



TPC<sub>Int</sub>. This might suggest that REML is a better indicator of depressive symptoms within a cluster, as opposed to a differentiator between symptom clusters. Future dimensional work in a larger population could elucidate similarities and differences in the mechanisms underlying lower REML between PTSD hyperarousal symptoms and depression.

### Hypothesis 2: Daytime and Sleep Measures of Arousal

REMD was expected to be positively correlated with all cluster symptoms, while HRV during REM sleep would be negatively correlated. Stronger correlations with hyperarousal and negative symptoms, and more moderate associations with intrusion and avoidance symptoms were predicted. Daytime measures of arousal, SCR negative and SCR neutral were expected to be more positively associated with hyperarousal scores than other symptom cluster scores.

As expected, all subscale scores were positively correlated with REMD, and negatively correlated with REM HRV. Hyperarousal and NegCog symptoms had the strongest positive correlation with REMD, suggesting that REM arousal is more pronounced in individuals with more severe NegCog or hyperarousal symptoms. Interestingly, and contrary to our hypotheses, intrusion and avoidance symptoms had the highest negative correlation with REM HRV. These findings should be analyzed cautiously due to the small sample size; however, these results may suggest that REM HRV and REMD measure different types of arousal, with REM HRV potentially being linked to daytime baseline stress.

Contrary to expectations, hyperarousal symptoms were strongly negatively correlated with SCR negative (SCR change from baseline to during trauma/nightmare

SDI), while intrusion scores were moderately correlated with SCR neutral (SCR change from baseline to during neutral SDI). This might reflect a ceiling effect, where individuals who have high baseline SCR values may have limited capacity for further increases in response to an intervention. This could potentially explain the negative correlational between hyperarousal symptoms and SCR negative, while intrusion symptoms were positively associated in change from baseline to SCR neutral due to lower baseline SCR. However, these results could support novel findings that SCR may be more closely related to expectations derived from pattern recognition rather than a measure of emotional response, and that within this framework, intrusive thoughts may be conditioned responses to trauma cues (Franke et al., 2021). This would potentially suggest that individuals who score highly in intrusive cluster symptoms are more susceptible to conditioning, and therefore recognize study-related patterns wherein the neutral SDI becomes a CS for the negative SDI (trauma or nightmare). Again, these findings are very preliminary and in a small population, and additional research is needed to uncover a convincing relationship between these variables.

### Hypothesis 3: Spectral Power Sleep Measures

For Aim 3, it was hypothesized that the hyperarousal cluster would have the most negative correlation with mean frontal REM theta and gamma power, and a positive correlation with mean frontal REM beta power compared to all other clusters.

While group differences did not reach significance, contrary to our expectations mean frontal REM beta power was lower in  $TPC_{Hyp}$  had compared to the  $TPC_{Av0}$  and  $TPC_{Int}$ . Research investigating beta power as a marker has thus far yielded inconsistent findings. Some literature suggest that beta power is a marker of hyperarousal or PTSD

severity (Germain, 2013; Germain et al., 2006; Jokić-begić & Begić, 2003). Our finding lends potential support to opposing literature showing that beta power during REM is negatively associated with self-reported hyperarousal and suggesting that beta power may be a measure of adaptive emotional processing (Denis et al., 2021; Goldstein et al., 2019; Mellman et al., 2017). Consistent with our hypothesis, mean frontal REM theta power was (non-significantly) lower in TPC<sub>Hyp</sub> compared with the TPC<sub>Av0</sub> and TPC<sub>Int</sub>. Frontal theta power during REM is higher in resilient individuals compared to those with PTSD (Cowdin et al., 2014), which may be related to its important role in the processing and consolidation of emotional memories (Hutchison & Rathore, 2015; Nishida et al., 2009). The observation in this study of simultaneously lower mean frontal beta and theta power during REM sleep in TPC<sub>Hyp</sub> may help substantiate the potential role of beta power in adaptive memory processing. Lower mean frontal beta and theta power in the TPC<sub>Hyp</sub> may point toward a greater role for aberrant emotional memory processing among individuals with more severe hyperarousal symptoms.

Consistent with the above findings, hyperarousal symptoms were most negatively associated with mean frontal theta power, followed by avoidance scores. This supports the SRSF Hypothesis, where hyperarousal may relate to a breakdown in salient memory processing. Intrusion and avoidance symptoms were weakly to moderately (non-significantly) correlated with mean frontal REM gamma power, which has been suggested as a measure of cortical arousal during sleep (Kang et al., 2014). These different patterns of frontal spectral power during REM sleep may suggest distinct contributions of emotional memory processing and arousal levels to the severity of specific PTSD symptom clusters.

#### Hypothesis 4: Self-Report Assessment Measures

The NegCog symptoms were expected to display the strongest association with depressive symptoms as measured by QIDS. Hyperarousal symptoms were expected to be most strongly associated with anxiety symptoms as measured by STAI-T. It was hypothesized that avoidance and intrusion symptoms would be most strongly associated with eveningness (lower MEQ score).

Hyperarousal symptoms exhibited strong, significant and near-significant correlations with QIDS and STAI-T and had higher (non-significant) mean scores on both assessments in pairwise comparisons. These findings highlight a robust link between heightened arousal and symptoms of anxiety and depression. While a relationship between hyperarousal symptoms and STAI-T was expected, the association with QIDS was unexpected. Yet more surprising was the weak, non-significant positive correlation between NegCog and QIDS; NegCog cluster scores actually showed a stronger positive correlation with STAI-T. This finding is consistent with analyses that demonstrate NegCog symptoms are not more significantly associated with depression than other symptom clusters, and that comorbidity between depression and PTSD is more related to general distress or negative affectivity (Byllesby et al., 2017).

All PTSD cluster symptoms were negatively correlated with MEQ, meaning that higher scores in all clusters were associated with eveningness. This makes sense in terms of the study population, since eveningness is associated with a higher propensity of nightmares (Nielsen, 2010; Selvi et al., 2012). Additionally, nightmares are one of the symptoms of the intrusion cluster, and in line with this, TPC<sub>Int</sub> had the highest mean MEQ score. TPC<sub>Av0</sub> had the second highest mean MEQ score, consistent another study

that found avoidance symptoms were strongly correlated with eveningness (Cruz-Sanabria et al., 2023). Surprisingly, NegCog symptoms had the one of the strongest negative correlations with MEQ. This is however consistent with literature found during analysis that shows that eveningness is associated with increased ruminative thinking (Antypa et al., 2017).

### MDS Solutions for Physiological and Subjective Measures

The MDS solution captures meaningful structure within the data, allowing for the accurate classification of subjects into distinct symptomatology clusters related to post-traumatic stress disorder (PTSD) features. These results contribute to our understanding of the interplay between sleep physiology variables and PTSD symptom clusters, highlighting the utility of MDS as a technique for identifying underlying structures in complex datasets. The observed predictive accuracy of the SVM model for both physiological measures (72.72%) and to a lesser extent subjective measures (62%) underscores the potential clinical relevance of the identified clusters, suggesting that certain patterns of sleep physiology or assessment variables may be associated with specific PTSD symptom profiles. Further research is warranted to validate these findings across larger and more diverse samples, as well as to explore the potential implications for tailored interventions targeting specific PTSD symptom clusters.

### REM Emotional Processing and Emotional Arousal

Heightened REM frontal theta power, indicative of increased emotional engagement and memory processing during REM sleep (Cowdin et al., 2014; Jones & Wilson, 2005; Nishida et al., 2009), is linked to a greater REMD. This finding potentially

suggests that a type of arousal during sleep, as measured by REMD, might be associated with dysfunctional memory processing.

Although the main effect of mean frontal REM gamma power did not reach statistical significance, the interaction effect between gamma and #REM (number of REM Periods) approached significance. This suggests a potentially nuanced influence of gamma on REMD that occurs within specific REM periods or deepens throughout the night. Varying numbers of REM Periods were significantly associated with distinct REMD values, emphasizing the importance of considering the temporal organization of REM sleep in understanding variations in emotional memory processing.

These findings illuminate the intricate connections between emotional memory processing, temporal dynamics of REM sleep, and REMD. Different emotional memory processes may unfold during different stages of REM sleep, which may have implications for overall sleep quality. Further research is warranted to delve into the specific mechanisms underlying these associations and their relevance for emotional and cognitive well-being during sleep.

### Study Limitations

Several limitations must be acknowledged in interpreting the findings of this study. Firstly, the small sample size likely caused many of the statistical analyses to be underpowered, leading to potential Type I and Type II errors.

Secondly, the small sample size also raises concerns about the generalizability of the results to broader populations. The predominantly female and younger demographic composition further restricts the general applicability of the findings, urging caution in extrapolating the outcomes to more diverse age and gender groups.

Thirdly, the variables here are “state” measures of sleep, taken primarily from one night of data. The lack of longitudinal data or repeated measures poses challenges in capturing the dynamic nature of sleep-related variables over time. Future research with larger, more diverse samples and longitudinal designs is crucial for validating and extending the current findings.

Lastly, it's important to note that the analyses did not control for the severity of symptoms on other assessment scales, such as the QIDS or STAI-T, when considering clusters. This limitation hinders a comprehensive understanding of the nuanced relationships between sleep measures and emotional well-being, emphasizing the need for more developed symptom-based analyses that account for the multifaceted nature of PTSD symptoms and their relationship with other mental health disorders.

### Conclusion

This study provides insights into the complex interplay between PTSD symptomology, sleep quality, affective memory processing, and mental health. The identified associations aim to contribute to a better understanding of the multifaceted underpinnings of sleep disturbances and their connections to the PTSD symptom clusters — and potentially other stress-related disorders. Future research may delve deeper into the specific mechanisms underlying these associations and explore targeted interventions and prevention strategies for improving both disordered sleep and PTSD.

## Appendix 1.

### Network Correlational Analysis

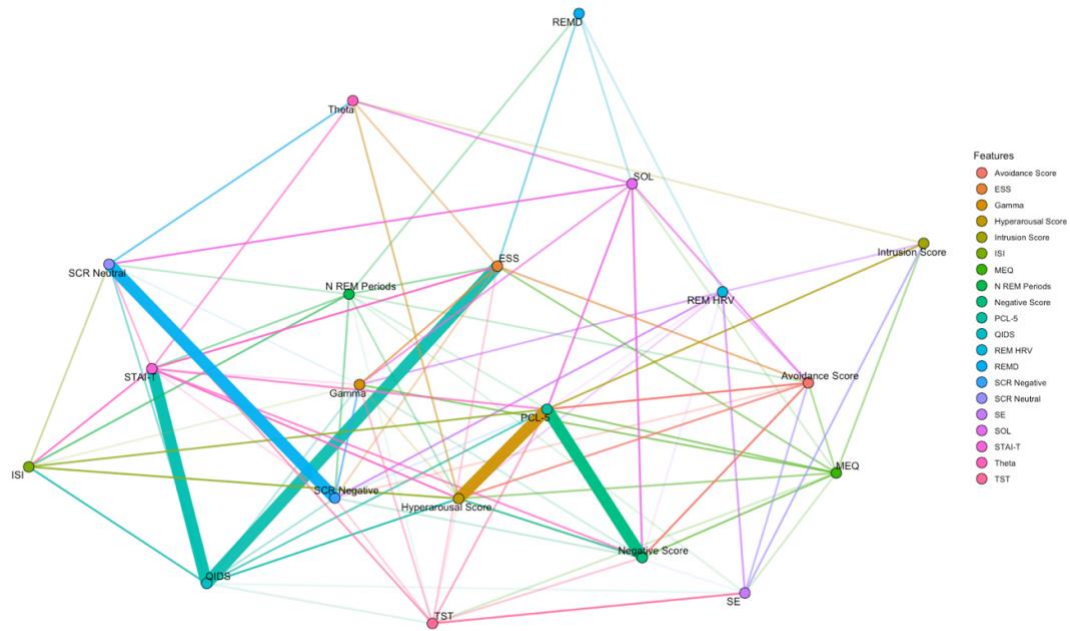


Figure 13. Complete Correlation Network.

*Network of pairwise correlations for all physiological and subjective measures. Strength of Spearman's  $\rho$  statistic correlation shown by saturation of line color connecting measures. Thick lines shown for significant p-values ( $p < 0.05$ ) after adjusting for multiple comparisons using the FDR method. Avoidance Score = mean PCL-5 avoidance subscale score. ESS = Epworth Sleepiness Scale. Gamma = EEG-measured frontal region brain activity in the gamma band range [ $\sim 30$  to  $100$  Hz]. Hyperarousal Score = mean PCL-5 hyperarousal subscale score. Intrusion Score = mean intrusion PCL-5 subscale score. ISI = Insomnia Severity Index. MEQ = Morningness-Eveningness Questionnaire. N REM Periods = total number of REM periods during PSG night. NegCog score = mean PCL-5 NegCog subscale score. PCL-5 = total score on the PTSD Checklist for DSM-5. QIDS = Quick Inventory of Depressive Symptomatology. REM HRV = RMSSD (root mean square of successive differences between RR intervals) measured during PSG night. SCR negative = skin conductance response during Nightmare or Trauma SDI. SCR neutral = skin conductance response during Neutral SDI. SE = sleep efficiency. SOL = sleep onset latency. STAI-T = Spielberger State Anxiety Inventory. Theta = EEG-measured frontal region brain activity in the theta band range [ $\sim 4$  to  $8$  Hz]. TST = total sleep time.*



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