

# *The Influence of PTSD on Circadian Rhythm*

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**Abstract:** The correlation between post-traumatic stress disorder (PTSD) and circadian rhythm disorders is bidirectional. Individuals with PTSD often experience disturbances in their sleep patterns, and abnormal rhythms can worsen PTSD symptoms through various biological mechanisms involving hormones and metabolism. Studies in neurobiology have shown that abnormalities in the adrenal axis among PTSD patients result in disrupted cortisol levels, which can directly impact the circadian rhythm control of the suprachiasmatic nucleus (SCN). When the autonomic nervous system is out of balance (with activity in the sympathetic nervous system), it can interfere with temperature regulation and heart rate variability. Imbalance can also lead to a reduction in hippocampus size. Increased amygdala activity affects how we perceive time and process emotions together. At the molecular level, trauma-induced changes in gene function, such as DNA methylation, can affect the regulation of circadian clock genes like BMAL1 and PER3, resulting in disrupted patterns of gene activity. Moreover, inflammation (increased IL-6 and TNF- $\alpha$  levels) and stress from oxidation worsen irregularities in energy processing due to faulty mitochondrial function. Medical approaches have evolved beyond therapies to manage rhythms effectively. In the future, researchers need to further explore how to better improve the circadian rhythm disorder of PTSD patients according to the existing shortcomings.

**Keywords:** Post-Traumatic Stress Disorder, Suprachiasmatic nucleus, Circadian Rhythm

## **1. Introduction**

Post-Traumatic Stress Disorder (PTSD) is a common mental illness caused by experiencing highly distressing events, such as the death of relatives, serious disasters, traffic accidents, sexual harassment, and assault. These stress-inducing events can trigger a series of changes in the brain, including the abnormal excitation of the sympathetic nervous system, which can lead to abnormal behaviors. PTSD patients often remain in a state of constant stress and exhibit high-alertness behaviors [1]. Stimuli related to stress events can cause strong physiological arousal reactions in PTSD patients, like elevated blood pressure and shortness of breath, as well as severe psychological disorders like emotional numbness and impaired emotional regulation. Simultaneously, patients also experience deficits in memory and sleep. They may have traumatic memory flashbacks, light sleep, frequent dreams, and nightmares. Research findings indicate that a small yet notable proportion, approximately 5%, of individuals diagnosed with PTSD endure short sleep episodes. In a 24-hour period, their sleep duration could fail to reach 6 hours. Furthermore, a significant percentage, ranging from 61% to 71% of PTSD patients, are plagued by nightmares that are directly linked to the stress-inducing events they have experienced. Similarly, insomnia is a prevalent issue among 51% to 61% of these PTSD patients,

significantly affecting their quality of life and overall well-being [2]. These psychological and physical symptoms are extremely distressing for patients and significantly impact the daily lives of both patients and their families.

The circadian rhythm is an endogenous 24-hour cycle of bodily function changes present in all living organisms. It is a crucial rhythm that enables organisms to adapt to variations in light intensity during the day-night cycle by regulating hormone secretion, sleep-wake cycles, and other factors. The circadian rhythm is regulated by multiple mechanisms. Organisms have a genetic basis for circadian rhythms; for example, in mammals, genes such as *Bmal1* and *CLOCK* are involved. The Suprachiasmatic Nucleus (SCN) is a key regulator of the circadian rhythm. It responds to light signals received from the retina, adjusting biological rhythms according to the external conditions [3]. Additionally, the SCN synchronizes the peripheral nervous system through neural signaling to maintain internal balance. One of the most prominent manifestations of the circadian rhythm is sleep. Upon detecting light, the SCN regulates sleep through multiple pathways, including modulating neurotransmitter secretion, transmitting sleep-related neural signals via connections with sleep-associated brain regions, and controlling the release of melatonin and cortisol".

PTSD patients often experience significant sleep disturbances, which can be attributed to multiple factors. First, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis disrupts cortisol and other hormone levels. Elevated cortisol may sustain a heightened state of alertness, impairing both the ability to fall asleep and maintain stable sleep. Second, autonomic nervous system dysfunction in PTSD patients further interferes with normal sleep patterns [4]. Third, psychological factors play a role—for instance, patients may avoid sleep due to fear of trauma-related flashbacks or distressing memories. Adequate sleep plays a crucial role in maintaining circadian rhythm stability. For PTSD patients, insufficient and irregular sleep can disrupt the secretion of melatonin, thereby impairing its regulatory influence on the circadian rhythm. Moreover, sleep also affects the secretion of other hormones, such as cortisol. When sleep is fragmented or inadequate, cortisol's natural secretion rhythm becomes dysregulated, further destabilizing the body's internal clock. Therefore, insufficient and irregular sleep disrupts the normal rhythm, destabilizes physiological homeostasis, and leads to metabolic dysregulation while impairing peripheral clock gene expression. These sleep-related disturbances further aggravate PTSD symptoms, perpetuating a harmful feedback loop. Crucially, the interaction between cortisol and sleep is bidirectional: elevated cortisol levels impair sleep quality, while sleep deprivation, in turn, exacerbates cortisol dysregulation, reinforcing a vicious cycle. This review explores the relationship between PTSD and circadian disruption, with the aim of informing targeted therapeutic interventions to improve physical and mental health outcomes in affected patients.

## **2. Molecular and genetic links between PTSD and circadian dysfunction**

The body's internal clock is controlled by a group of genes, such as *BMAL* and *CLOCK*. It can be disrupted by the disorder of the expression of these genes. For example, research has shown changes in the expression levels of *BMAL1* and *CLOCK* genes in PTSD patients, as well as disturbances in *PER* and *CRY* proteins. Such molecular alterations can disrupt the rhythm of our body clocks, leading to issues like sleep problems, being overly alert, and experiencing mood swings, often seen in people with PTSD [5]. And traumatic experiences can lead to changes in our genes through modifications, which can impact the body's clock function negatively over time.

Inflammation and oxidative stress also play a crucial role in the development of PTSD, closely associated with circadian rhythm disturbances as well. Research has shown increased levels of inflammatory cytokines and interleukin can impact the body's internal clock by disrupting the expression of genes responsible for regulating circadian rhythms. For example, *IL-5* has been demonstrated to inhibit the expression of *BMAL0* whereas *TNF-α* could disturb the expression

patterns of PER3 [6]. This interference with cytokines' rhythms may play a role in sleep disturbances and changes in stress reactions observed in individuals with PTSD.

One characteristic of PTSD is that stress further exacerbates disruptions in the body's internal clock. When people experience trauma, their body may produce reactive oxygen molecules, leading to issues with the energy-producing mitochondria and disrupted metabolism. Mitochondria are important in keeping cells energized and balanced for rhythms to work right. Stress-induced damage to DNA and proteins impairs ATP production, disrupting clock gene activity and circadian rhythm misalignment [7]. This disturbance in energy production could also play a role in the tiredness and cognitive issues frequently observed in individuals with PTSD. According to the above understanding of the treatment mechanism of circadian rhythm in patients with PTSD, scientists have developed many methods to treat circadian rhythm disorders. For example, temporal therapy, including strong light irradiation and blue light-blocking glasses, effectively resets the circadian rhythm and enhances melatonin production. Pharmacological interventions such as melatonin, ramelteon, and beta blockers aim to achieve circadian resynchronization and reduce excessive arousal. Behavioral strategies such as CBT-I and mindfulness can also stabilize sleep. These combined methods provide promising avenues for circadian rhythm adjustment and sleep improvement [8].

### 3. Neurobiological basis of PTSD and circadian rhythm disruptions

Research has clearly demonstrated that dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis in individuals with PTSD [9]. This neuroendocrine system functions through coordinated interactions between the hypothalamus, pituitary gland, and adrenal glands to regulate the body's stress response. During stressful events, the hypothalamus secretes corticotropin-releasing hormone (CRH), which stimulates the anterior pituitary to release adrenocorticotrophic hormone (ACTH). Circulating ACTH then activates the adrenal cortex to produce cortisol. This hormonal cascade induces a heightened state of physiological arousal, preparing the body for adaptive responses to environmental challenges. A key consequence of this activation is transient immunosuppression, which prioritizes immediate threat response over immune function [10]. Under normal conditions, the HPA axis maintains a precisely regulated circadian rhythm of cortisol secretion [6]. Stress responses can be categorized into distinct patterns, with particular relevance to PTSD patients who experience acute stress exposure. Such traumatic events can induce significant neurobiological changes, resulting in persistent hyperactivity of the stress response system and a transition to chronic stress states. This pathological condition leads to frequent activation of the HPA axis, establishing a maladaptive feedback loop. Substantial evidence confirms that prolonged stress exposure impairs both cognitive function in animal models and proper regulation of the HPA axis.

Cortisol serves as a critical modulator of circadian function, interacting with the body's timing system to influence clock gene expression in peripheral tissues across circadian timescales [11]. Hormones exert regulatory effects on the suprachiasmatic nucleus (SCN) through multiple pathways, including indirect modulation via their influence on secondary hormones and neurotransmitters. Notably, cortisol affects melatonin secretion—a process intrinsically linked to SCN function and fundamental to circadian rhythm regulation. The disrupted cortisol secretion patterns characteristic of HPA axis dysregulation may significantly impair the body's sleep-wake cycle. PTSD also can significantly disrupt autonomic nervous function, affecting both sympathetic and parasympathetic activity. Experimental evidence demonstrates markedly reduced parasympathetic reactivity in PTSD patients, as measured by heart rate variability (HRV), a sensitive indicator of parasympathetic modulation [12]. Psychological studies further reveal that parasympathetic function during REM (Rapid Eye Movement) sleep exhibits distinct abnormalities in PTSD patients, closely associated with their hyperarousal symptoms. In healthy individuals, the parasympathetic nervous system maintains moderate tension during REM sleep to regulate physiological processes. In contrast, PTSD patients

show significantly diminished parasympathetic tone during this phase, which may underline their exaggerated arousal responses.

The neurobiological connection between PTSD and circadian disturbances primarily involves three key regions: the amygdala, prefrontal cortex (PFC), and hippocampus. Under normal conditions, these structures work in concert to regulate stress responses, emotional processing, and circadian synchronization [13]. However, in PTSD patients, dysfunction in these key brain regions directly disrupts circadian rhythm regulation. The amygdala shows pathological hyperactivity, resulting in exaggerated fear responses while simultaneously impairing the prefrontal cortex's ability to modulate both stress reactions and circadian timing. Hippocampal degeneration, which is associated with impaired memory consolidation, additionally disturbs temporal perception. These neural alterations collectively destabilize the sleep-wake cycle, creating a feedback loop that intensifies core PTSD symptoms.

#### **4. Sleep disturbances in PTSD and their circadian basis**

Individuals with PTSD may struggle with sleep-related issues such as difficulty falling asleep and fragmented sleep patterns that disrupt their overall sleep quality [14]. One noticeable symptom often observed in individuals with PTSD is a delay in the onset of sleep, which results in reduced sleep duration compared to those without the condition. Moreover, they may experience a prolonged period before falling asleep after attempting to do so, which could be linked to their emotional state and reluctance to enter the sleeping phase. The patient's nervous system is in a state and filled with intrusive trauma-related thoughts that hinder their ability to sleep well and enter a deep state of relaxation during restorative sleep cycles. Invasive, distressful memories may manifest as dreams while one is asleep, disrupting the usual sleep pattern and hindering individuals from attaining restful and adequate sleep quality. Their ability to sleep well is significantly diminished with an average efficiency of less than 70% [15]. Moreover, the rise in the frequency of waking up at night among individuals intensifies the disturbance in their sleep patterns. Studies using polysomnography have unveiled intricate alterations in sleep patterns. The findings indicate an extension in the duration of N1 (light sleep) among patients while the amount of slow-wave sleep. Vital for the body's physical restoration is notably diminished.

During the slow-wave sleep (SWS) deep sleep, the body undergoes various crucial physiological regulation and repair processes, like stimulating growth hormone secretion to boost immunity and repair tissues. However, this is significantly disrupted in the PTSD patients, leading to adverse effects on their overall well-being and daily functioning. Physiologically, one important factor contributing to sleep disturbances in PTSD is the increased alertness caused by the hyperactivity of noradrenergic neurons in the locus coeruleus, which is a region of the brain with a gathering of neurons, regulating brain excitation and relaxation.

During the nighttime, the body follows a circadian rhythm that is regulated by an internal clock, gradually decreasing wakefulness and facilitating sleep. Nevertheless, heightened noradrenergic activity in the locus coeruleus persistently stimulates the sympathetic nervous system, disrupting the natural decrease and alerting the circadian rhythms in PTSD patients. As a result, PTSD patients may struggle to initiate sleep at night and experience frequent nighttime awakenings, even when they manage to fall asleep. REM sleep imbalance is another hallmark of PTSD-related sleep disturbances, characterized by an increase in REM density and disruption in the processing of emotional memories. Studies show that a significant percentage of PTSD patients frequently experience trauma-related nightmares during the REM sleep stage, which suggests difficulties in fear extinction function among these patients. Neuroimaging research has linked this issue to heightened activity (responsible for processing fear and emotions) in the amygdala and reduced activity in the cortex. Moreover, the increased activity of norepinephrine greatly affects REM sleep. High levels of norepinephrine in

REM sleep can disturb the balance of the circuit, making nightmares more vivid and memorable [16]. Melatonin is a hormone that helps regulate our sleep-wake cycle and is primarily controlled by the SCN (suprachiasmatic nucleus). People with PTSD often experience disruptions in their sleep patterns, including a delayed release of melatonin from the pineal gland in the brain.

Healthy individuals with normal melatonin levels typically rise as night approaches, peaking at an optimal time to signal the body to prepare for sleep. However, PTSD patients tend to experience the peak of melatonin secretion approximately 2 to 3 hours later than in those without the condition. This delay in melatonin release disrupts the body's natural sleep cues and further leads to a prolonged period of transition between sleep and waking up for these patients. The consequence is often difficulty falling asleep at bedtime and heightened brain activity during night hours. The regular cycle of core body temperature plays a crucial role in the body's circadian rhythm and serves as an indicator for assessing the circadian rhythm and the overall balance of the body's functions [17]. Typically, body temperature fluctuates throughout the day, regulated by the circadian rhythm and external influences. For instance, a gradual decrease in body temperature in the evening helps signal the body to prepare for sleep. Nonetheless, PTSD patients often experience disruptions in the rhythm of their core body temperature, leading to reduced temperature fluctuations and a weakened rhythm, making it difficult to fall asleep or have a night's sleep.

The autonomic nervous system plays a role in regulating body temperature. The reduction in the control of nerves impacts the balance of body temperature and leads to disturbances in the rhythm of the body temperature cycle. PTSD patients experience disturbances in the rhythm of their core body temperature for reasons such as reduced parasympathetic control during sleep in those with more severe symptoms [18]. Furthermore, anomalous cortisol secretion in individuals with PTSD (due to circadian rhythm discrepancies) impacts the hypothalamus and influences the center responsible for regulating body temperature. Psychological elements also contribute to the body's temperature pattern. The disturbance of rhythms and core body temperature rhythms mutually influence each other, creating a harmful feedback loop. Social jet lag occurs when there is a mismatch between the body's clock and daily routines. This effect is especially noticeable in people with PTSD because their delayed melatonin release changes their sleep-wake cycle. That throws off the body's internal clocks, which are found in organs like the liver, responsible for breaking down substances, and adipose tissue, which stores energy and controls metabolism.

## 5. Conclusion

In conclusion, scientists do know that there is a bidirectional, very obvious association between PTSD (Post-Traumatic Stress Disorder) and circadian rhythm disorders. The symptoms of the disease exacerbate gene disorders and hormonal secretion disorders, which are sleep disorders in PTSD patients. This, in turn, exacerbates the circadian rhythm disorders. Conversely, the circadian rhythm disorders exacerbate hormonal imbalances, and so on. Despite the identification of the disease, numerous questions remain unanswered, particularly regarding treatment. For instance, we can do more longitudinal studies to gain more understanding of the pathogenic mechanisms; we can specifically study patients of different genders and see the difference; and finally, we can look into the possibility of gene therapy that acts on the circadian rhythm pathway (through the integration of various research strategies), and so on. Based on these findings, healthcare providers will be in a better position to individualize treatments to improve the quality of life and the outcomes of patients.

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