Palliative Medicine: The Importance of Sleep, Stress, and Behavior

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Abstract

With the growing research that sleep habits interact with stress and health, it is now essential to understand exactly how sleep influences stress, which contributes to a person’s overall health and wellness. This is equally important for palliative medicine care. Stress has been shown to play an active role in health, while sleep has been shown to effect levels of stress. Those who are experiencing poorer sleep, also experience more stress, which potentially leads to risk of various health concerns. Therefore, it is essential to understand the interworking relationship between stress and sleep in order to effectively maximize restorative sleep for the best health outcomes.

The present article examines the relationship between stress and sleep, along with extra consideration to potential factors that could be mediating the aforementioned relationship. Gaining an understanding of these relationships may assist future research and treatment developments for sleep deficiency and resulting health consequences during palliative care.

Keywords: Palliative Medicine; Sleep; Stress; Behavior; Health Effects; Circadian Rhythm; Sleep Regulation; Cortisol Level

Introduction

Recent studies have indicated that Cortisol, a main hormone of stress, plays a critical role in the development of habitual behavior. For instance, it has been shown that stress induces a shift in the control of instrumental behavior from goal-directed to habitual responses [1]. The term “stress” was coined by Hans Selye, who defined it as “the non-specific response of the body to any demand for change” [2]. A stressor is more recently defined as environmental change which increases catecholamine hormones or cortisol, that have a variety of effects on the body [3]. Allostatic load/overload refers to the cumulative “wear and tear” on body systems caused by too much stress and/or inefficient management of the systems that promote adaptation through allostasis [4]. The endogenous level of cortisol varies according to an individual’s circadian rhythm. In humans, cortisol levels are low at midnight and increase overnight to a peak in the morning. Following this morning peak, cortisol levels slowly decline throughout the day [5].

Sleep is a state of immobility which consists of greatly diminished physical responsiveness that allows for the rejuvenation of neural activity [6,7]. Although some research supports sleep as a buffering system [8], there is also support for sleep deprivation as a stand-alone stressor instead of a moderator [9]. Sleep deprivation affects cognitive functioning across a number of domains, including, but not limited to: attention; information-processing speed; psychomotor reaction time; working memory; learning and immediate memory recall; abstract reasoning; inhibition of previously learned responses and impulses; and decreased awareness to present situations and circumstances [10]. Sleep loss has also been shown to be associated with a diminished quality-of-life [11] and increase economic costs [12]. Overall, sleep deprivation has also been found to be associated with short- and long-term negative consequences for health and wellbeing, including increased risk of cardiovascular disease and mortality [13, 14]. It is extremely important to consider these relationships even during palliative care.

Sleep

Individual-sleep needs vary widely among individuals; still, most sleep experts recommend seven to nine hours of sleep each night [15]. However, nearly 30% of all adults sleep less than six hours a night [16]. There are two most-widely accepted theories of separate types of processes used to regulate sleep. The first, the Homeostatic Sleep-Regulating Process consists of a need to sleep that compounds during hours of wakefulness and is then brought to a homeostatic level during sleep. The other system, the Circadian Rhythm Sleep-Regulating Process consists of internal bodily processes that regulate a more week-based timing of feelings of sleepiness [17-20].

There is also support that acute stress and sleep loss may alter diurnal cortisol rhythms [21, 22]. Sleep-quality and sleep-quantity have been shown to be distinct individual outcomes. More recent findings began measuring in terms of sleep-quality because it better controlled varying sleep groups. It is more important how little disruption and deep sleep an individual receives (sleep-quality) than purely how many hours one sleeps (sleep-quantity) [23-25]. The remainder of the findings concentrates on sleep-quality instead of quantity, as it is a better control for sleep. Insufficient and disturbed sleep is linked with...
adverse health conditions, including cardiovascular disease [26], obesity [27], Type 2 Diabetes [23], hypertension [28], and depression [29]. The period of peak sleepiness shifts earlier after young adulthood. Overall sleep quantity and the amount of time spent in the non-rapid eye movement (REM) stage diminish as an individual gets older [30]. This holds some concerns for age as a moderator for sleep quality.

**Physiological Health**

In regard to physical health, changes in sleep patterns causing significant loss of sleep increase pain sensitivity, which interferes with pain-relieving treatments [31], and cause low-grade cardiovascular inflammation [26]. It has been found that chronically painful events have been frequently associated with disturbances in sleep, which involves increased daytime sleepiness and changes in sleep quality and continuity [106]. The relationship between sleep and pain involves several simultaneous unidirectional and/or bidirectional interactions between sleep and pain which can then alter pain perception [31, 107-109]. Recent epidemiological data shows that the general population experiences substantial increases in “next-day pain frequency” when transitioning from a night of relatively normal sleep (6-9 hours) to a night of either fewer than 6 hours or greater than 9 hours of sleep [110, 111]. This puts emphasis on the system that regulates our daily sleep.

**Circadian rhythm** is a system which guides the internal schedule of sleep for most animals including humans, and it is often the first system disrupted by stress [32]. Studies have shown that, even with a small disruption (e.g., a few days) of circadian rhythm, there are increases in physiological responses (e.g., appetite, blood pressure, levels of pro-inflammatory cytokines, and evening-cortisol levels), as well as decrease parasympathetic response [4, 33, 34]. Beyond these acute effects, chronic circadian disruption is associated with increased likelihood of obesity, elevated cortisol, and overall shrinkage of the temporal lobe [4]. Individuals reporting sleep problems also evidence lower overall health quality [35, 36], and greater physical-health problems, such as muscle pain, headaches, and gastrointestinal problems [36]. In addition to these findings for basal cortisol levels, a recent review has further suggested that poor sleep, in particular if prolonged, may also interfere with acute endocrine stress responses [37].

**Psychosocial Health and Palliative Care**

In terms of psychosocial health, sleep loss influences the secretion of hormones (e.g., cortisol) which can influence mood and contribute to anxiety disorders [38, 39]. When sleep-quality diminishes the parasympathetic system is compromised causing the individual to start the next day with a higher baseline level of cortisol that continues building throughout the day. As cortisol level rise throughout the day, as they normally would, the effects that cortisol have on the body take effect [38, 39]. This can vary depending on the interpretation of the sleep loss for the individual, those that perceive more helplessness to their loss of sleep typically have more drastic hormone changes [110, 111].

Also, poor sleep has been shown to impair the processing of recent emotional experiences that occur overnight [40] and reduce the accuracy with which people recognize emotions [41]; which explains sleepiness and negative affective states [42]. There is also support that chronic sleep deprivation causes memory to be impaired, along with increases in oxidative stress [4]. Even though all these problems have been found with a lack-of-sleep, it is suggested that sleep problems might contribute towards these adverse health effects by negatively influencing the stress system. Specifically, elevated-stress responses [43], as well as attenuated responses of the stress system [37], can be maladaptive for health, and poor sleep is related to both heightened and attenuated endocrine stress responses [44, 45].

**Stress**

Stress is a negative emotional experience accompanied by anticipated biochemical, physiological, cognitive and behavioral responses that are directed either toward altering the stressor or accommodating to their effects. Animal studies have shown that chronic social stress disrupts sleep regulation, causing an exacerbated wakefulness period and an over-active sleep cycle in mice [46]. This is speculated to have a similar effect for humans. However, it is difficult to experimentally test the effects of chronic stress on human behavior because it is ethically difficult to control. However, there is support that job-work stress is a strong risk factor for depressive symptoms, with those who are experiencing pre-existing sleep disturbances [47]. A review based on high-quality studies on the relationship between work and sleep found indications that lack of control and psychosocial demands at work may lead to poorer subsequent sleep-quality [48].

Work stress has also been shown to decrease quality-of-sleep, and positive methods for addressing stress show it to help sleep quality [49, 50]. Brain regions which are involved in memory and emotions (e.g., hippocampus, amygdala, and prefrontal cortex) undergo structural-remodeling when subjected to chronic stress, with the result that memory is impaired and anxiety and aggression are increased [4]. Stress can also lead to problems with health-habit forming behaviors; it is more difficult to form habits due to hormonal interference from cortisol [51]. The endogenous level of cortisol varies according to an individual's circadian rhythm. In humans, cortisol levels are low at midnight, and increase overnight to a peak in the morning. Following this morning peak, cortisol levels slowly decline throughout the day [5].

Stress activates the hypothalamic-pituitary-adrenal (HPA) axis to regulate physiological responses to stressors [52, 53]. The HPA-axis responses to stress are also modulated by several individual and contextual factors (e.g., age, gender, time of day) [54, 55]. Several studies suggest that poor sleep is associated with atypical cortisol reactivity to psychosocial stress among both children [44, 56, 57, 58] and adults [45, 59]. Sleep behavior is closely linked with the HPA axis, as optimal sleep (in terms of duration and quality) is associated with a healthy diurnal profile of cortisol release as indicated, for example, by higher levels of cortisol in the morning, its lower concentration in the...
evening, and a steeper slope of cortisol secretion [60]. Atypical cortisol reactivity associated with poor sleep is most likely what moderates HPA-axis response changes from sleep deprivation [61]. Relatedly, experimental and population-based research tested the plausible impact of sleep deprivation and fragmentation on basal-levels of cortisol, an important biomarker of the HPA axis [62], and numerous studies reported elevated as well as blunted cortisol concentrations [63, 64, 65]. Elevated cortisol levels have been found to be associated with conditions such as Type 2 Diabetes [66] and all-cause mortality [67], while blunted cortisol responses have been reported in clinical populations, including patients with depression [68] or chronic fatigue [69].

Cyclical Reactivity

The findings discussed above support that sleep can influence stress. Prolonged lack of sleep can raise, as well as blunt, cortisol concentrations resulting in increased health concerns (e.g., Type 2 Diabetes) or depression, respectively (e.g., poor sleepers reported greater perceived stress-reactivity levels, even after adjustment for age and body mass index [70]). However, cortisol and perceived stress reactivity were not independent of BMI, chronic stress levels, and endocrine; also, generally perceived stress reactivity was dissociated from sleep disturbance [71]. Initially, self-report data supported that there was a cyclical reactivity between sleep and stress. However, with further investigation, it has been shown that there is not a cyclical reactivity effect, and that good-sleep leads to less stress, while poor-sleep leads to more stress. Modifying poor sleeping habits typically greatly improves salivary free cortisol [71]. This modification should always be considered in palliative medicine.

Potential Confounds

Positive Affect

Basic motivational theories of emotion provide a general model that helps link the experience of emotion, both positive and negative, with health-related outcomes. The background idea of these models is that emotions exist in the service of motivating behavior or promoting particular action-tendencies [72, 73]. Emotional motivation theory led to the finding that the resulting actions and biological responses may provide a respite from the stress associated with negative affectivity [74, 75] specifically with biofeedback measures of cardiovascular reactivity [76-78]. Prolonged neuroendocrine response to stress has also been associated with depressed mood [79], while lower levels of cortisol found in saliva have been associated with measures of well-being [80]. Therefore, the association between neuroendocrine function and emotional responding is also a potential mechanism linking positive emotion to physical-health outcomes.

Job Stressors

Workers often attribute poor-sleep to factors at work. Sleep problems experienced by workers have additional public health consequences. There are correlations between poor quality-of-sleep and accidents, including incidents in the workplace [81-83] as well as motor vehicles accidents [83, 84]. Employers bear additional costs due to sleep-related productivity losses, which may reach another $50 billion per year [12]. Sleep disorders are also associated with lower job performance, greater absenteeism, and increased use of sick leave [85, 86], which affect increased costs. Also, there are additional costs due to increased health care utilization [86], such as doctor visits and hospitalization [87]. In the US, insufficient sleep of employees caused an estimated $150 billion in indirect costs in 2010 (combined costs of absenteeism, presenteeism, and workplace accident or injuries [88, 12]).

Jobs create stress which, in turn, causes a lack of restorative sleep. Workers who are overloaded with work were associated with poorer sleep-quality, and those that reported experiencing monotonous repetition in their jobs showed non-restorative sleep [89]. Recent systematic reviews of work and sleep shows that high-work demands (e.g., job strain, bullying, and effort-reward imbalance) were related to more future sleep disturbances, while psychosocial work variables (e.g. social support at work, control, and organizational justice) were related to fewer sleep disturbances [90]. Therefore, job stress is associated with sleep ability, which could generate more stress for the individual, as well as lead to cyclical reactivity from lack of good sleep (even though stress and sleep have been supported as not having cyclical reactivity as discussed above [71]).

Age

There are several different contributors which can diminish sleep in an aging population. Adults tend to have poorer sleep quality, and sleep for less overall time, which interrupt fully recuperative sleep, and benefits cannot be fully acquired [91]. Older adults (7-8 hours a night) typically require less sleep than younger adults (8-9 hours), and even less than children (9-11 hours [92]). Still, adults get less sleep than the already low recommended sleep. One common problem with loss of sleep due to aging is the circadian rhythm mechanisms that change due to old age [93]. Loss of sleep also contributes to neurodegeneration, which is a key component in dementia. Neurodegeneration is not associated with old age, but it is associated with loss of regenerative sleep which is linked with old age [94]. Due to the intimate relationship between circadian rhythm interruption and neurodegeneration, it is essential to manage sleep effectively and get as much restful, rejuvenating sleep as possible, especially in older adults undergoing palliative care.

Depression

There is still a great deal that is unknown about the associations between depression, stress, and sleep problems. Stress and depression have been found to be correlated for both undergraduate and graduate students [95] and stress has been evaluated as both a predictor of depressive symptomatology and as a predictor of sleep problems [95, 96]. Despite the typically strong associations between stress and depression, they consistently emerge as two independent constructs [97]. The literature is mixed regarding the causal direction between these affective factors and sleep, and there is evidence that the associations may be bidirectional in nature [98, 99]. It is difficult
to jointly predict stress, depression, and sleep problems, or if poor sleep patterns (including the quality- and quantity-of sleep) predict stress and/or depression. However, there is potential for depression mediating stress and sleep. Although there are potentially more mediators, there is little structured research on other strong variables that may be associated (this is not considering medical disorders that directly affect sleep). However, more recently, Lyall et al. (2018) have found that a disrupted circadian clock was related to mood disorders, such as lifetime bipolar disorder and major depression disorder.

Conclusion

In the United States, there are national programs aimed at promoting stress-reducing habits in working adults (e.g., National Healthy Worksite Program by the Centers for Disease Control and Prevention, 2018), as well as promoting good sleeping-habits (e.g., National Sleep Foundation, 2018). This is not surprising given the important roles that stress and sleep play in human daily functioning and health. Acute stress responses are also influenced by other factors such as physical exercise [100] and chronic stress [101]; both of these are also linked with sleep quality and vice versa [102-104]. Thus, there is much support from the research discussed above which shows that stress affects sleep restoration and regulation. Research also supports that sleep-quality, rather than sleep-quantity, may be the greater health concern for young adults [105]. This suggests that intervention programs targeting depression, stress management, and healthy sleep-patterns should be investigated. This is equally important for patients undergoing palliative care.

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