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Review Article

Sleep: The Linchpin of Hormone Regulation? A Literature Review

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Abstract

Healthy sleep can modulate hormone levels which affect an individual's overall health. The quality and quantity of a person's sleep are important indicators of the changes in hormone levels in the body and of the severity of an individual's non-transmittable chronic health conditions, moods, energy level, and disease processes. Several hormone levels that are known to fluctuate during sleep include: insulin, leptin, ghrelin, testosterone, progesterone, cortisol, melatonin, and serotonin. An evaluation of how sleep stabilizes the body's multiple hormone levels reveals the importance of sleep; these hormone levels depend on high quality and quantity sleep to keep an individual healthy. A review of the literature reveals how sleep is the driving regulator of all of the body's hormone levels. Sleep efficiency is also an indicator of high quality sleep. The literature review resulted from a search of databases that included: PubMed, EBSCOhost, Access Medicine, Medscape, and DynaMed using key words: sleep, sleep hygiene, sleep efficiency, sleep quality index, sleep and each hormone listed (insulin, leptin, ghrelin, testosterone, progesterone, cortisol, melatonin, and serotonin). The total number of articles included in this review is 38; after evaluating the abstracts and full text of 124 articles, 67 were excluded for being similar and 19 were eliminated as not relevant. Future research into other hormones altered by sleep loss should include: cholecystokinin, glucagon-like peptide-1 (GLP-1), peptide YY, orexin, neuropeptide Y, adipokines, dopamine and thyrotropin.

Keywords: Healthy sleep; Hormone levels; Sleep efficiency; Sleep hygiene

Introduction

The purpose of this review is to evaluate the link between adequate rejuvenating sleep every night and an individual's level of health, based on a stable level of the body's multiple hormone levels achieved during sleep. The hormones evaluated for this article with regard to how sleep affects them include: insulin, leptin, ghrelin, testosterone, progesterone, cortisol, melatonin, and serotonin.

The rationale for evaluating sleep is that an individual spends 4 to 10 hours of their time each day sleeping vs diet/eating (1 to 3 hours), or exercise (30-60 min/day). Improving a person's diet and exercise have traditionally been the focus on how to improve an individual's health; improving a person's sleep focuses on several health aspects simultaneously.

In the past 50 years there have been major health changes in non-communicable chronic diseases in the population. Diabetes now affects 9% of all adults; heart disease affected 17.5 million people in 2012; obesity affects 642 million people; depression affects 350 million people [1]. All of these chronic diseases are negatively affected by a lack of sleep. Researchers are increasingly linking Type 2 diabetes and obesity to lack of sufficient sleep. This loss of sufficient sleep is a problem not just for adults, but also for children who are raised in today's modern society [2]. Also "short sleep duration has been shown to be associated with elevated body mass index (BMI)" [2]. When an individual sleeps for "less than 7 hours per day it is associated with an increased risk of obesity, diabetes, high blood pressure, heart disease, stroke, and frequent mental distress" [2].

Coincidently during the past 50 years, the rise in the use of electronics and light in the evening has also increased, while the time spent asleep has decreased to less than 6 hours per night for 30-44% of all adults, with night shift workers most affected by fewer hours of sleep [3]. Children are sleeping 1.2 hours less, which tends to be more of a problem on school nights [3].

Sleep Quality, Quantity and Efficiency

To create dramatic changes in an individual's health there has to be an underlying current that creates those changes. When the individual hormones are examined in response to sleep restriction and low sleep quality, the larger picture of health effects emerges. The main areas of health emphasized in discussions with patients generally include questions regarding diet and exercise. But if the patient is also questioned about his or her quality and quantity of sleep, what they practice for stress reduction, and what their sleep efficiency is, then a fuller view of the individual's health appears. Research shows sleep regulates or changes several hormones. This paper reviews eight of the hormones affected by a loss of high quality and quantity sleep.

In evaluating the quantity of sleep, less than 5½ hours of sleep is detrimental, whereas the ideal total number of hours asleep in bed is 8½ hours [4]. When an individual sleeps for less than 5½ hours it is more difficult to lose weight and to have stable levels of leptin and ghrelin [4].

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When an individual improves sleep quantity and quality, glucose regulation and metabolic rate greatly improves [5]. Sleep quality can be evaluated based on how rested individuals feel when awake. When sleep quality is low the resulting fatigue may affect insulin levels as well. High fatigue levels can lead to overeating, increased weight, less initiative to exercise, and more unstable insulin levels. When evaluating sleep quality, a provider should also assess sleep efficiency. Sleep efficiency is the time asleep divided by the time in bed. Researchers have found that "sleep quality and sleep efficiency, had a stronger association with BMI than did sleep duration" and that inconsistent sleep patterns and poor sleep efficiency were related to adiposity [6]. A lack of ability to stay asleep all night is stressful and fatiguing, and leads to increases in cortisol and ghrelin, followed by an increase in weight.

Sleep quantity varies by individual, with a range of 4-10 hours per night. Problems occur when the quantity of sleep falls below 6 hours of sleep per night including: the risk of obesity, a larger waist circumference, cardiovascular disease, Type 2 diabetes, and risk of accidents [6]. Most individuals feel best with 7-8 hours of sleep per night; sleeping 7-8 hours per night is also associated with individual's weighing the least [6]. The improved weight can be related to improved insulin, leptin, ghrelin, and cortisol regulation. Sleeping less than the recommended 7-8 hours per night for an adult is one of the leading indicators of increased weight gain and obesity [6].

Hormones Changed by Sleep Loss

The hormone Leptin is responsible for helping an individual feel full or satiated after eating. When an individual feels satiated, eating stops and the ability to maintain a stable, healthier weight can be achieved. But when an individual is sleep deprived, the cravings for more energy dense and higher calorie food increases. The individual has low energy and thinks that eating more food will provide the energy needed to successfully accomplish tasks throughout the day [7]. This increased caloric consumption leads to weight gain and a decreased sensitivity of the body's ability to detect the activity of the hormone leptin, which can then develop into leptin resistance when an individual practices yo-yo dieting [8].

Low leptin and high ghrelin levels are associated with short sleeping hours (five hours vs. eight hours) [6]; and "restricted sleep duration was found to be associated with reduced leptin levels independently of BMI" [9]. Leptin resistance is also associated with insulin resistance, and has been seen in rats after being overfed for three days [10]. The ability of an individual to overeat high energy dense foods in modern society is easy. Once an individual's taste buds have become accustomed to eating in a certain way it can take extreme effort to change those learned behaviors. Health education and support makes it easier for individuals to be successful in learning how to eat balanced, nutritious meals that enable an individual to feel full. Sleep hygiene education teaches an individual how to achieve the highest quality sleep so that leptin hormone levels will not be sensed by the body as too low, causing an individual to overeat. When sleep time is shortened there is an "associated decrease in circulating levels of leptin (anorexigenic hormone)" [11]. The decrease in leptin along with satiety level also affects the ability of insulin to work well in the body, which can lead to overeating to combat the high fatigue level.

The hormone ghrelin is an appetite stimulant. The hormones that are directly related to an individual's hunger and satiety level are: ghrelin (hunger) and leptin (satiety) [7]. Some of the lifestyle factors that affect ghrelin hormone levels include: changing work shifts, sleep restriction, and loss of sleep. Ghrelin helps the body regulate the use of energy from food by adjusting the hunger signals to balance with an individual's energy output [12]. When ghrelin hormone levels are lower, an individual will be less likely to overeat, or feel cravings to overeat.

When an individual exhibits short sleep cycles, it creates high levels of ghrelin in the body, which is also associated with obesity due to the high levels of perceived hunger [13]. The energy level of an individual who has been able to obtain an ideal amount of sleep tends to be higher without the need for an increased amount of food. This resulting energy balance from increased hours of sleep allows the individual to achieve a lower BMI without the discomfort associated with dieting. Ghrelin also works with dopamine to regulate the reward perception within the brain, which helps an individual feel calmer [14].

Insulin is the hormone which regulates the metabolism of carbohydrates and fats in the body [15]. The ability of the body to regulate insulin levels is considerably affected by sleep loss.When sleep time is reduced, there is an association of insulin resistance, impaired glucose tolerance, and increased risk of type 2 diabetes [11]. When the individual is able to adhere to a regular, non-sleep-depriving, sleep schedule, insulin levels are more stable and the A1C blood parameter also improves.With improved sleep quantity and quality, glucose regulation and metabolism greatly improves [5].

Cortisol, the stress hormone, is often called the "fight or flight" hormone which prepares an individual to survive a dangerous situation. Stress levels increase an individual's cortisol and insulin hormone levels in the blood at the same time. When an individual experiences shortened sleep time, evening concentrations of cortisol increase, which in turn increases the level of ghrelin [16]. The resulting higher stress level can cause some individuals to overeat in the evening. The overeating, low quality sleeping, and higher stress levels create an unhealthy vicious cycle. Normally there is a rise in cortisol in the morning that peaks within the first 30 minutes of an individual waking, then the cortisol gradually decreases throughout the day [17]. The findings of increased cortisol in the evening is the newest abnormal hormone indication of stress, with the subsequent health challenges of raised plasma glucose and insulin resistance associated with a future diagnosis of diabetes [17].

Sleep restriction increases cortisol stress hormone levels in just six consecutive nights. In Spiegel's study the participants slept for four hours per night, during six nights and showed an elevated evening cortisol level and growth hormone level, and reductions in thyroid-stimulating hormone [9]. There was also a slower return to normal for the cortisol level the day following sleep restriction (simulating night shift work) even though the participants did not perceive an increase in stress [9]. The added stress of shift work with successive loss of sleep hours might be something to consider when applying for a job.

Testosterone is the primary male hormone. It is normal for levels

of testosterone to rise at sleep onset for men, and peak with the first REM-sleep episode (especially for younger men) but older males experience a 0.2—2% annual decline in morning testosterone as they age [18]. As males grow older and testosterone declines, (starting between ages 30 and 40) more problems with shortened sleep time and sleep problems occur [19]. Consecutive blood tests reveal that "lower levels of circulating testosterone were associated with reduced sleep efficiency, increased time awake after sleep onset, decreased number of REM-sleep episodes, greater latency of the first REM-sleep period, and poorer sleep quality associated with lower testosterone concentrations" [19].

There are several benefits of testosterone including: improved muscle mass, strength, bone density, vigor and decreased adiposity [20]. It appears that high sleep quality is important to maintain levels of testosterone. Several studies have confirmed that obstructive sleep apnea (OSA) and sleep fragmentation reduce testosterone levels, but when a continuous positive airway pressure (CPAP) device is utilized, testosterone levels improve [20]. Physical activity improves sleep architecture while increasing testosterone (and mood) and decreasing progesterone levels, which decreases a female's risk for breast cancer [21,22].

Progesterone is one of the primary female hormones. Progesterone levels in women fluctuate monthly, which can challenge most researchers. Women who are taking contraceptive hormones are usually excluded from studies due to their confounding effects [19]. There are several life stages that women go through that affect hormone levels, including: pregnancy, peri-menopause, and menopause. When progesterone levels are not stable, women might not feel as well. Progesterone can create a "hypnotic, benzodiazepine-like effect on sleep EEG in rodents" [19]. For women with sleep challenges, "progesterone treatment alone led to decreased time spent awake and increased REM-sleep in the first third of the night" [23].

For pregnant women there tends to be more sleep challenges with loss of sleep being associated with higher rates of preterm labor, longer and more painful labor, preeclampsia, caesarean section, and a greater risk of postpartum depression [19,24]. Sleep hygiene educational tips can decrease these problems. When a younger person is sleep deprived, they present physiologically at an older level, equal in metabolic and endocrine function to an older healthy adult with no sleep loss [25].

Melatonin is a hormone that helps regulate an individuals sleep and waking schedule. Melatonin levels naturally rise in the evening, (and stay elevated for about 12 hours) which make an individual sleepy. With the rise in use of electronic blue light emitting devices in the evening, especially in the hour before bedtime, however, a significant reduction in melatonin is created [26,27]. The reduction in melatonin can be attenuated by wearing blue blocker glasses while watching any blue light device in the evening, but there is still a reduced level of alertness the next morning [26,27]. There are some individuals who will opt to take a melatonin pill in an attempt to counteract the effects of blue light, but caution is warranted, as there can be significant health challenges caused by taking a melatonin pill without consulting a physician first [28]. Although there are promising studies in which melatonin has been proven safer than other medications, and with fewer side affects, it could be useful for sleep behavior disorder, Alzheimer's disease, and the elderly [29,30].

Raising melatonin levels through high quality sleep also helps prevent cancer, and improves oxidative stress from heart attacks and strokes [31]. The timing of cancer treatment is affected by the time of day a drug is administered, due to the circadian rhythm of stem cells [32]. Improving exposure to natural light in the daytime can increase the level of melatonin. Studies have shown that by working near a window, melatonin blood levels were increased at night, cortisol was decreased, depression was decreased, and there was improved quality of sleep [33]. Another non-medication treatment to raise melatonin levels includes, eating a high tryptophan breakfast under bright light to produce higher melatonin levels at night [34].

The hormone serotonin is important for helping to regulate an individual's mood, appetite, sleep, and depression. When serotonin levels are too low, eating disorders, irritable bowel syndrome, clinical depression, and REM sleep disorders occur [35]. Too little sleep decreases an individuals energy level, which in turn drives the craving for sweets (vs. the high tryptophan whole foods) which leads to more fatigue, overeating, and inadequate sleep [36]. In addition to improving what an individual eats, adding bright light exposure also improves serotonin levels [37].

Serotonin levels can be raised by eating a high tryptophan diet in the daytime, since tryptophan is transformed into serotonin in the brain, then converted into melatonin in the evening [34,36]. Since 90% of serotonin is synthesized in the intestinal tract, eating a high tryptophan diet will enhance an individuals ability to absorb more serotonin, which in turn creates more melatonin and a better nights sleep [38]. Another key ingredient to increasing an individual's serotonin level naturally is by engaging in physical activity. Exercise increases the ability of the body to synchronize sleep-wake cycles, which is accompanied by an increase in serotonin in the brain, creating improved sleep at night, but this benefit ceases when the individual stops exercising [21].

Conclusion

The importance of sleep is underestimated by most individuals. Evaluating sleep as being the driving force in balancing out and regulating the hormones of the body may be a new concept for patients. One of the most important topics healthcare providers should counsel patients about is to practice sleep hygiene, and provide sleep health education tips to ensure a high quality and quantity sleep. It is important for the population to understand the linchpin qualities of sleep and how an individual's health can be affected by a loss of high quality and quantity sleep. The benefit of following sleep hygiene health behaviors enables an individual to live a high quality life while decreasing chronic health disease risk. Other lifestyle stressors that are not always evaluated that might confound the data include: "socio-economic status, physical activity level, alcohol consumption, caffeine consumption, mood, and psychological disorders" [6]. All of these stressors can affect the quality and quantity of sleep and deserve attention.

Further evaluation should determine the time frame of a drop in sleep quality or quantity and when chronic disease will appear. More research is necessary to evaluate the importance of sleep efficiency and how this percent relates to the amount of hormone changes

from sleep. Additional research into other hormones altered by sleep loss should examine the effects of: cholecystokinin, glucagon-like peptide-1 (GLP-1), peptide YY, orexin, neuropeptide Y, adipokines, dopamine and thyrotropin. Sleep efficiency percent should become a standard vital sign.

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