SHODH SAGAR®
International Journal for Research Publication and Seminar
ISSN: 2278-6848 | Vol. 15 | Issue 3 | Jul - Sep 2024 | Peer Reviewed & Refereed

Recent advances in sleep cycle regulation and hormonal imbalance: a comprehensive review

Sheersh Jain*
sheershjain1597@gmail.com

DOI: https://doi.org/10.36676/jrps.v15.i2.1412
Published: 01/07/2024

* Corresponding author

1. Introduction:

A vital physiological function, sleep is necessary for general health and wellbeing. It is essential for several body processes, including as metabolism, immunological response, emotional control, and cognitive function. A complicated mechanism involving intricate connections between brain circuits, neurotransmitters, and hormone cues governs the sleep-wake cycle. Scientific research has recently made significant progress in understanding the mechanisms behind the control of the sleep cycle and how it relates to hormone imbalance. The goal of this thorough review is to examine the most recent research in this area, with a particular emphasis on the interaction between hormone variations and sleep regulation.

A circadian rhythm, an internal biological clock that synchronizes with the day-night cycle, controls the sleep-wake cycle. The hypothalamus's suprachiasmatic nucleus (SCN) acts as the body's master pacemaker, regulating the timing of several physiological functions, such as alertness and sleep. The main environmental cue that synchronizes the circadian rhythm is light, which tells the brain to start sleep at night and encourage awake throughout the day. The function of particular genes and chemicals in controlling the circadian rhythm has been clarified by recent research, providing information on possible treatment targets for sleep problems.

Moreover, there is a close connection between the homeostatic control of sleep and the sleep-wake cycle. By blocking neuronal pathways that encourage alertness, the neurotransmitter adenosine—which builds up in the brain during waking—promotes sleep. On the other hand, when you sleep, your body produces less adenosine, which makes it easier for neurotransmitters that promote alertness to take over, such dopamine and acetylcholine, when you wake up. A better understanding of the mechanisms behind sleep regulation has been made possible by the discovery of novel neurotransmitter systems and brain circuits that are involved in the control of sleep homeostasis in recent research.

The commencement, maintenance, and quality of sleep are all important features of the sleep-wake cycle that are influenced by hormones. Women's sleep patterns can be greatly impacted by changes in hormone levels during the menstrual cycle, pregnancy, menopause, and aging. For instance, the structure and quality of sleep are influenced by the reproductive hormones progesterone and estrogen. Progesterone has calming properties that aid in deeper, more restorative sleep, whereas estrogen encourages REM sleep. However, hormonal fluctuations during the menstrual cycle and menopausal transition can disrupt sleep continuity and quality, leading to sleep disturbances such as insomnia and sleep fragmentation.

In a similar vein, changes in thyroid hormone levels may impact the control of sleep. Low thyroid hormone levels are the hallmark of hypothyroidism, which is marked by symptoms including excessive daytime drowsiness, exhaustion, and poor sleep quality. On the other hand, hyperthyroidism, which is characterized by high thyroid hormone levels, can cause increased REM sleep and insomnia. The

processes underpinning the reciprocal link between thyroid function and sleep have been clarified by recent studies, underscoring the significance of thyroid hormone balance in preserving sound sleep patterns.

Furthermore, the main stress hormone, cortisol, is essential for controlling the sleep-wake cycle. Cortisol levels have a diurnal cycle; they increase in the morning to encourage awake and decrease during the day to help with the beginning of sleep. Chronic stress, on the other hand, and dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis can throw off this pattern, resulting in sleep disorders such insomnia and fragmented sleep. According to new research, people with chronic stress may benefit from mindfulness-based therapies and stress-reduction strategies to help balance their HPA axis and get better sleep.

Hormonal imbalance and sleep regulation interact in a reciprocal manner; disturbances in one system frequently impact the other. Lack of sleep, for instance, can change the levels of the hormones cortisol, ghrelin, and leptin, which can result in increased hunger, weight gain, and metabolic problems. On the other hand, conditions like insulin resistance and polycystic ovarian syndrome (PCOS) can result in hormonal imbalances, which in turn can cause sleep disorders including insomnia and sleep apnea.

Furthermore, new research points to the possibility that sleep disruptions worsen hormonal imbalances and hasten the onset of metabolic diseases including diabetes, obesity, and cardiovascular disease. It has been demonstrated that sleep loss alters glucose metabolism, resulting in insulin resistance and decreased glucose tolerance. Furthermore, hormones that control appetite can be dysregulated by sleep deprivation, resulting in heightened appetite and a desire for high-calorie meals.

Our awareness of the complex interaction between hormone imbalance and sleep cycle control has deepened due to recent developments in scientific study. Hormonal signals, neurotransmitter systems, and the circadian rhythm work together dynamically to regulate when and how well people sleep. Women's sleep patterns can be greatly impacted by hormonal changes throughout the menstrual cycle, pregnancy, and menopause. Thyroid function changes and cortisol levels can also cause disturbances in men's and women's sleep-wake patterns. To clarify the underlying processes and create focused therapies for sleep problems linked to hormone imbalance, more study is required. Clinicians can enhance overall health and well-being and maximize treatment results by addressing hormonal health and sleep.

2. Objectives

- To investigate the mechanisms underlying the bidirectional relationship between sleep cycle regulation and hormonal imbalance.
- To evaluate the impact of hormonal fluctuations on sleep patterns and quality.
- To examine the role of specific hormones in modulating various aspects of the sleep-wake cycle.
- To assess the potential implications of sleep disturbances on hormonal balance and metabolic health.
- To explore potential therapeutic interventions and management strategies targeting both sleep disorders and hormonal imbalances.

3. Relationship between sleep cycle regulation and hormonal imbalance

The bidirectional relationship between sleep cycle regulation and hormonal imbalance is a complex interplay that involves intricate physiological mechanisms. Understanding these mechanisms is crucial for elucidating the underlying causes of sleep disturbances and hormonal imbalances and developing

effective therapeutic interventions. This section will delve into the key mechanisms driving this bidirectional relationship.

3.1 Neuroendocrine Interactions:

Central to the bidirectional relationship between sleep and hormones are neuroendocrine interactions involving the hypothalamus, pituitary gland, and various hormone-producing glands throughout the body. The hypothalamus serves as a critical hub for integrating signals from the internal and external environment to regulate both sleep-wake cycles and hormone secretion. For instance, the hypothalamic-pituitary-adrenal (HPA) axis, which governs the stress response, plays a significant role in regulating cortisol secretion and modulating sleep patterns. Cortisol levels follow a diurnal rhythm, peaking in the early morning to promote wakefulness and declining throughout the day to facilitate sleep onset. Disruptions in this rhythm, such as those induced by chronic stress, can lead to alterations in sleep architecture and quality.

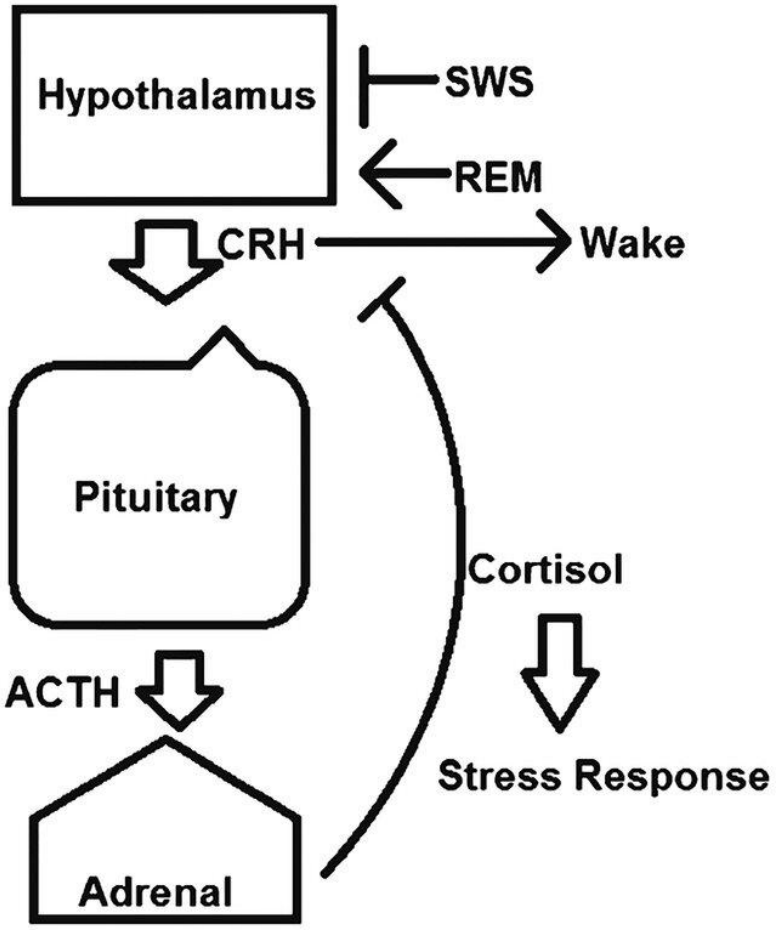

Figure: Neuroendocrine Interactions (Source: Smith and Mong, 2019)

3.2 Circadian Rhythm Regulation:

The circadian clock, located in the suprachiasmatic nucleus (SCN) of the hypothalamus, orchestrates the timing of various physiological processes, including sleep and hormone secretion. Light exposure serves as the primary synchronizing signal for the circadian clock, helping to align internal rhythms with the day-night cycle. Disruptions in the circadian rhythm, such as those induced by shift work or jet lag, can dysregulate hormone secretion and disrupt sleep patterns. For example, alterations in the

timing of melatonin secretion, a hormone involved in the regulation of sleep-wake cycles, can contribute to sleep disturbances and hormonal imbalances.

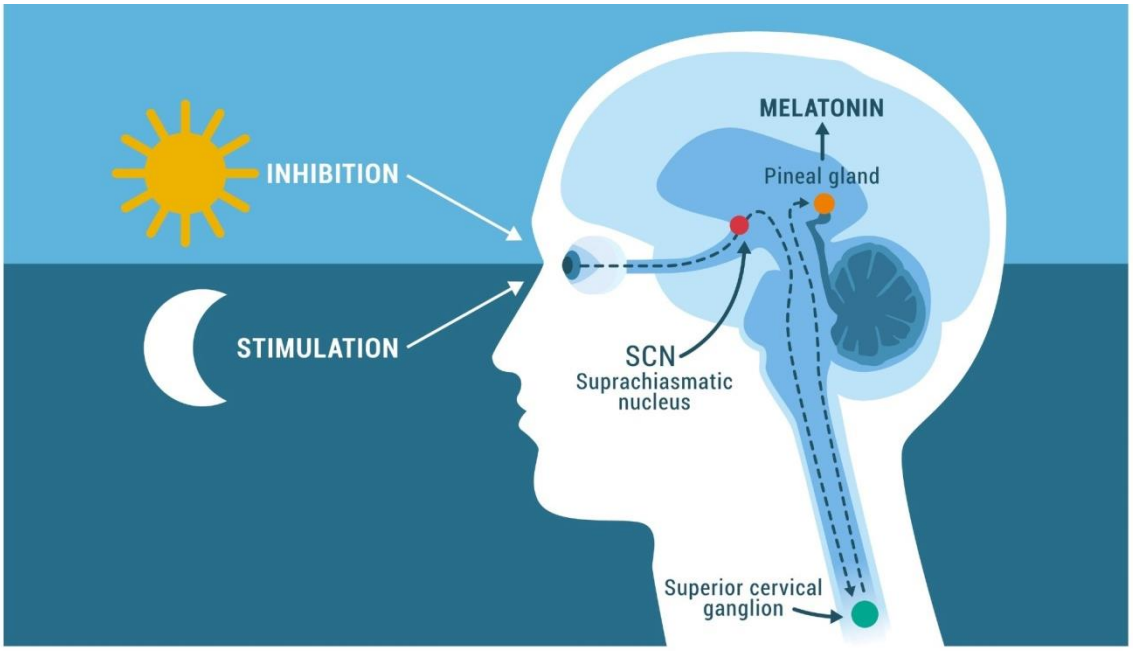

Figure: Circadian Rhythm (Source: https://www.news-medical.net/health/Sleep-and-Hormones.aspx)

3.3 Hormonal Feedback Loops:

Hormonal feedback loops play a crucial role in maintaining homeostasis within the endocrine system and regulating both sleep and hormone secretion. For instance, the hypothalamic-pituitary-gonadal (HPG) axis regulates the secretion of reproductive hormones such as estrogen and progesterone, which in turn, influence sleep patterns and quality. Estrogen has been shown to promote REM sleep, while progesterone has sedative effects, contributing to deeper and more restorative sleep. Conversely, disruptions in reproductive hormone levels, such as those occurring during the menstrual cycle or menopausal transition, can lead to sleep disturbances and hormonal imbalances.

3.4 Metabolic Regulation:

Sleep plays a crucial role in regulating metabolic processes, including glucose metabolism, appetite regulation, and energy balance. Hormones such as insulin, leptin, and ghrelin play key roles in these processes and are tightly regulated by sleep-wake cycles. Sleep deprivation has been shown to disrupt glucose metabolism, leading to insulin resistance and impaired glucose tolerance. Additionally, insufficient sleep can dysregulate appetite-regulating hormones, leading to increased hunger and cravings for high-calorie foods. Conversely, metabolic imbalances such as obesity and diabetes can impact sleep quality and duration, further exacerbating hormonal disturbances.

3.5 Inflammatory Pathways:

Emerging evidence suggests that inflammatory pathways play a significant role in mediating the bidirectional relationship between sleep and hormones. Chronic inflammation has been implicated in the pathogenesis of various sleep disorders and hormonal imbalances. For example, sleep disturbances such as sleep apnea and insomnia have been associated with elevated levels of pro-inflammatory cytokines, which can disrupt hormone secretion and exacerbate metabolic dysfunction. Conversely, hormonal imbalances such as insulin resistance and polycystic ovary syndrome (PCOS) have been linked to chronic inflammation, further exacerbating sleep disturbances and metabolic dysfunction.

The bidirectional relationship between sleep cycle regulation and hormonal imbalance is governed by a complex interplay of neuroendocrine interactions, circadian rhythm regulation, hormonal feedback loops, metabolic regulation, and inflammatory pathways. Disruptions in any of these mechanisms can lead to sleep disturbances and hormonal imbalances, which, in turn, can exacerbate each other and contribute to the development of various health conditions. Understanding these mechanisms is essential for developing targeted interventions to improve sleep quality, regulate hormone secretion, and optimize overall health and well-being.

4. Impact of hormonal fluctuations on sleep patterns and quality

Hormonal fluctuations during key reproductive stages such as the menstrual cycle, pregnancy, and menopause significantly impact sleep patterns and quality in women. Understanding the effects of these fluctuations is essential for managing sleep disturbances and promoting overall well-being during these life stages.

4.1 Menstrual Cycle:

Hormonal changes during the menstrual cycle, particularly fluctuations in estrogen and progesterone levels, can influence sleep patterns. The menstrual cycle consists of two main phases: the follicular phase, characterized by rising estrogen levels, and the luteal phase, marked by increased progesterone levels. Research suggests that sleep architecture may vary across these phases, with some women experiencing alterations in sleep duration, sleep efficiency, and subjective sleep quality. For example, some studies have found that women may experience more fragmented sleep and increased wakefulness during the luteal phase, possibly due to the sedative effects of progesterone. Additionally, fluctuations in estrogen levels have been associated with changes in REM sleep, with some women reporting more vivid dreams and increased REM sleep duration during certain phases of the menstrual cycle. Overall, the menstrual cycle can impact sleep patterns and quality, although individual variations exist.

4.2 Pregnancy:

Pregnancy is accompanied by profound hormonal changes, including increases in estrogen, progesterone, and prolactin levels, which can significantly impact sleep patterns and quality. During the first trimester, hormonal fluctuations, along with physical discomforts such as nausea and frequent urination, may contribute to sleep disturbances such as insomnia and fragmented sleep. Additionally, hormonal changes can lead to alterations in sleep architecture, with some women experiencing decreased REM sleep and increased awakenings during the later stages of pregnancy. The third trimester, in particular, is associated with challenges such as discomfort due to fetal movements and changes in sleeping positions, further exacerbating sleep disturbances. Hormonal fluctuations postpartum, including the abrupt decline in estrogen and progesterone levels, can also disrupt sleep patterns and contribute to postpartum insomnia and mood disturbances.

SHODH SAGAR®
International Journal for Research Publication and Seminar
ISSN: 2278-6848 | Vol. 15 | Issue 3 | Jul - Sep 2024 | Peer Reviewed & Refereed

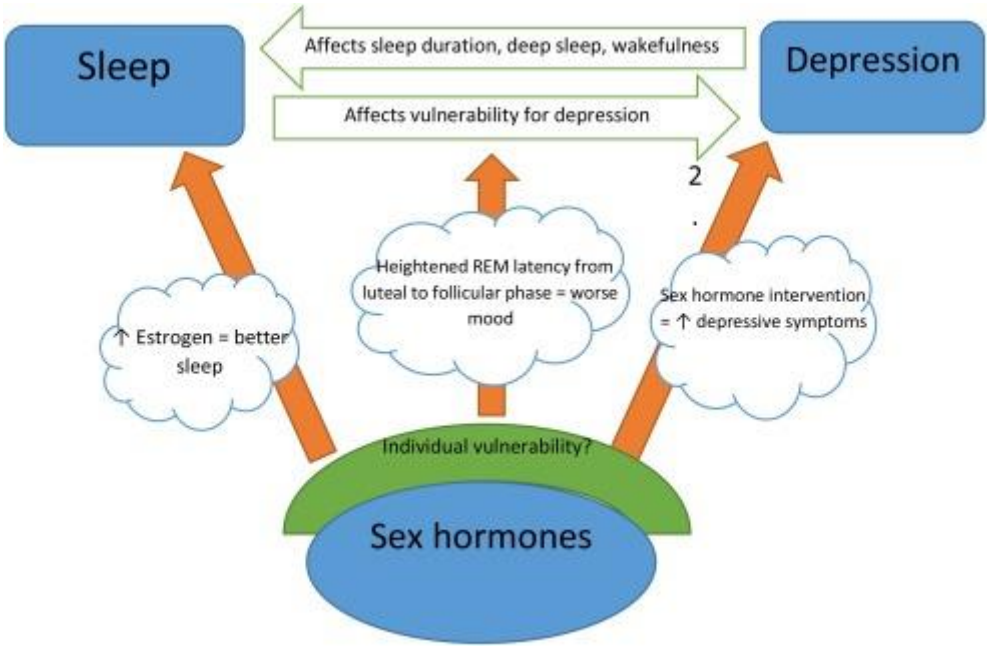

Figure: Interactions between sleep, depression and sex hormones (Source: Morssinkhof et al 2020)

4.3 Menopause:

Menopause marks the end of reproductive function and is characterized by a decline in estrogen and progesterone production. Hormonal fluctuations during perimenopause, the transitional period leading up to menopause, can contribute to sleep disturbances such as insomnia, night sweats, and hot flashes. Estrogen plays a role in thermoregulation, and its decline is thought to contribute to the onset of vasomotor symptoms such as hot flashes, which can disrupt sleep continuity and quality. Additionally, changes in sleep architecture, including reductions in REM sleep and slow-wave sleep, have been observed during menopausal transition. Hormonal therapy, aimed at restoring estrogen levels, is often prescribed to alleviate menopausal symptoms and improve sleep quality. However, the benefits and risks of hormone therapy should be carefully considered based on individual health status and preferences.

4.4 Impact on Overall Well-being:

The impact of hormonal fluctuations on sleep patterns extends beyond mere inconvenience, significantly affecting overall well-being and quality of life. Chronic sleep disturbances associated with hormonal fluctuations can lead to daytime fatigue, irritability, mood swings, cognitive impairment, and decreased productivity. Additionally, sleep disturbances during reproductive stages such as pregnancy and menopause may exacerbate existing physical discomforts and emotional stressors, further impacting mental and emotional health. Addressing sleep disturbances during these life stages is crucial for promoting maternal health during pregnancy, supporting women's health during menopause, and improving overall quality of life.

Hormonal fluctuations during key reproductive stages such as the menstrual cycle, pregnancy, and menopause can significantly impact sleep patterns and quality in women. Understanding the effects of these fluctuations is essential for managing sleep disturbances and promoting overall well-being during these life stages. Effective management strategies may include lifestyle modifications, stress reduction techniques, behavioral interventions, and, in some cases, hormonal therapy. By addressing sleep disturbances associated with hormonal fluctuations, healthcare providers can help improve women's quality of life and overall health during these critical life stages.

5. Role of hormones in modulating sleep-wake cycle

Specific hormones play crucial roles in modulating various aspects of the sleep-wake cycle, including initiation, maintenance, and quality of sleep. Understanding the roles of these hormones provides insights into the complex interplay between endocrine regulation and sleep physiology.

5.1 Estrogen:

Estrogen, a primary female sex hormone, exerts profound effects on sleep architecture and quality. Research suggests that estrogen influences both the timing and duration of sleep across the menstrual cycle, pregnancy, and menopausal transition. During the menstrual cycle, estrogen levels rise during the follicular phase and peak just before ovulation. Estrogen has been shown to enhance REM sleep, the stage of sleep associated with vivid dreams and memory consolidation. Additionally, estrogen may contribute to the regulation of circadian rhythms, influencing the timing of sleep onset and wakefulness. However, fluctuations in estrogen levels, particularly during perimenopause and menopause, can lead to sleep disturbances such as insomnia and fragmented sleep. Hormonal therapy aimed at restoring estrogen levels may help alleviate menopausal symptoms and improve sleep quality in some women.

5.2 Progesterone:

Progesterone, another female sex hormone, plays a crucial role in promoting sleep and modulating sleep architecture. During the menstrual cycle, progesterone levels rise during the luteal phase, following ovulation. Progesterone has sedative effects and is thought to contribute to deeper and more restorative sleep. Research suggests that progesterone increases the duration of non-REM sleep, the stage of sleep associated with physical restoration and repair. Additionally, progesterone may help regulate body temperature and reduce the frequency of nocturnal awakenings. However, fluctuations in progesterone levels, particularly during the menstrual cycle and menopausal transition, can disrupt sleep continuity and quality. Hormonal therapy may be beneficial for some women in alleviating sleep disturbances associated with progesterone deficiency.

5.3 Thyroid Hormones:

Thyroid hormones, including thyroxine (T4) and triiodothyronine (T3), play a critical role in regulating metabolism, energy expenditure, and thermoregulation, all of which influence sleep-wake cycles. Thyroid hormones are involved in the maintenance of body temperature, with optimal thyroid function essential for the regulation of circadian rhythms and sleep-wake cycles. Hypothyroidism, characterized by low levels of thyroid hormones, is associated with symptoms such as excessive daytime sleepiness, fatigue, and poor sleep quality. Conversely, hyperthyroidism, marked by elevated thyroid hormone levels, can lead to insomnia, increased REM sleep, and heightened arousal. Proper management of thyroid disorders is essential for restoring thyroid hormone balance and improving sleep quality.

5.4 Cortisol:

Cortisol, the primary stress hormone, plays a crucial role in regulating the sleep-wake cycle and maintaining wakefulness. Cortisol levels follow a diurnal rhythm, peaking in the early morning to promote wakefulness and declining throughout the day to facilitate sleep onset. Cortisol is involved in the regulation of the circadian clock and helps synchronize internal rhythms with the day-night cycle. Additionally, cortisol acts as a counter-regulatory hormone, opposing the effects of sleep-promoting neurotransmitters such as adenosine. Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, which controls cortisol secretion, can lead to disruptions in cortisol rhythms and sleep disturbances such as insomnia and fragmented sleep. Chronic stress and elevated cortisol levels have been associated with sleep disorders and metabolic dysfunction, highlighting the importance of stress management in promoting healthy sleep.

Estrogen, progesterone, thyroid hormones, and cortisol play distinct yet interconnected roles in modulating various aspects of the sleep-wake cycle. Fluctuations in hormone levels, whether physiological or pathological, can significantly impact sleep architecture, duration, and quality. Understanding the intricate interplay between endocrine regulation and sleep physiology is essential for developing targeted interventions to manage sleep disturbances and optimize overall health and well-being. Hormonal therapy may be beneficial for some individuals in restoring hormone balance and improving sleep quality, although the risks and benefits should be carefully considered based on individual health status and preferences.

6. Implications of sleep disturbances on hormonal balance

Sleep disturbances can have profound implications for hormonal balance and metabolic health, contributing to the development of obesity, diabetes, and cardiovascular disease. The bidirectional relationship between sleep and hormones, along with their interconnected influence on metabolic processes, underscores the importance of addressing sleep disturbances to mitigate the risk of these metabolic disorders.

6.1 Impact on Hormonal Balance:

Sleep disturbances, such as insufficient sleep duration, poor sleep quality, and sleep disorders like sleep apnea, can disrupt hormonal balance through multiple pathways. One of the key hormones affected by sleep disturbances is cortisol, the primary stress hormone. Chronic sleep deprivation and disrupted sleep patterns can lead to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, resulting in elevated cortisol levels throughout the day. Elevated cortisol levels have been associated with insulin resistance, abdominal obesity, and metabolic syndrome, contributing to the development of type 2 diabetes and cardiovascular disease.

6.2 Insulin Resistance and Glucose Metabolism:

Sleep disturbances, particularly short sleep duration and poor sleep quality, have been linked to insulin resistance and impaired glucose metabolism. Sleep plays a crucial role in regulating glucose homeostasis, with sleep deprivation leading to decreased insulin sensitivity and impaired glucose tolerance. Insulin resistance, in turn, contributes to the development of type 2 diabetes, a metabolic disorder characterized by high blood sugar levels. Moreover, sleep disturbances have been associated with alterations in appetite-regulating hormones such as leptin and ghrelin, leading to increased hunger, cravings for high-calorie foods, and dysregulated energy balance, further exacerbating metabolic dysfunction.

6.3 Obesity and Weight Gain:

Sleep disturbances have been implicated in the development of obesity and weight gain, partly through their effects on appetite regulation, energy balance, and metabolic rate. Short sleep duration and poor sleep quality have been associated with increased appetite, food cravings, and consumption of energy-dense foods. Moreover, sleep deprivation alters the balance of hormones involved in appetite regulation, leading to increased levels of ghrelin, a hunger-stimulating hormone, and decreased levels of leptin, a satiety hormone. These hormonal changes promote overeating and weight gain, contributing to the development of obesity and metabolic syndrome.

6.4 Cardiovascular Disease Risk:

Sleep disturbances have been identified as independent risk factors for cardiovascular disease, including hypertension, coronary artery disease, and stroke. Chronic sleep deprivation and sleep disorders such as sleep apnea have been associated with elevated blood pressure, inflammation, endothelial dysfunction, and dyslipidemia, all of which contribute to the development and progression of cardiovascular disease. Additionally, sleep disturbances can disrupt autonomic nervous system

function, leading to increased sympathetic activity and reduced parasympathetic activity, further exacerbating cardiovascular risk.

6.5 Inflammatory Pathways:

Sleep disturbances are associated with increased systemic inflammation, which plays a central role in the pathogenesis of obesity, diabetes, and cardiovascular disease. Chronic sleep deprivation and disrupted sleep patterns have been shown to upregulate pro-inflammatory cytokines and downregulate anti-inflammatory cytokines, leading to a state of chronic low-grade inflammation. Inflammatory pathways contribute to insulin resistance, endothelial dysfunction, atherosclerosis, and plaque rupture, increasing the risk of metabolic disorders and cardiovascular events.

Sleep disturbances can have significant implications for hormonal balance and metabolic health, contributing to the development of obesity, diabetes, and cardiovascular disease. Addressing sleep disturbances through lifestyle modifications, behavioral interventions, and, when necessary, medical treatments is essential for mitigating the risk of these metabolic disorders and improving overall health and well-being. By recognizing the intricate interplay between sleep, hormones, and metabolism, healthcare providers can develop targeted interventions to optimize sleep quality, restore hormonal balance, and reduce the burden of metabolic diseases.

7. Recent advances in sleep study

As a domain under heightened scrutiny as of recent times, significant strides have been made in the study of sleep. This has been a massive boon to the millions of patients world wide suffering from disorders related to sleep.

One of the many frightening conditions related to sleep is apnea. It is a chronic disease where breathing is periodically interrupted when asleep. Recently, a scalable method of determining physiological endotypes of sleep apnea from a polysomnographic sleep study has been developed that is cheaper and does not require as much technical expertise as before. The standard method utilizes python reprogramming to endotype sleep apnea from a polysomnogram. This method(PUP) developed by Sands et al. is computationally expensive and requires technical expertise to run. Its re-implementation(PUPpy), developed by Finnsson et. al-which is computationally cheaper and more accessible to researchers- was validated by comparing the testing data with the results of the (PUP) method and found to be accurate.

This is allowing more and more researchers who are interested in endotyping but have not been able to due to extreme pre-requisites to contribute to the study.

Another important advancement is the newfound relationship between cardiovascular diseases and sleep. The LS7(American heart association's life simple 7) which are the 7 parameters that are used to score a person's cardiovascular health have had no mention of sleep until now. They have the following parameters(excluding sleep):

Table 1 (source: American heart association)

Cardiovascular health metric	Ideal (score=2)	Intermediate (score=1)	Poor (score=0)
Smoking	Never smoker	Former smoker	Current smoker

Diet	Meets 4–5 recommendations	Meets 2–3 recommendations	Meets 0–1 recommendations
Physical activity	≥150 min/wk moderate intensity or ≥75 min/wk vigorous intensity or ≥150 min/wk moderate+vigorous intensity	1–149 min/wk moderate intensity or 1–74 min/wk vigorous intensity or 1 to 149 min/wk moderate+vigorous intensity	No moderate or vigorous activity
BMI	<25 kg/m^2	25–29.9 kg/m^2	≥30 kg/m^2
Blood pressure	SBP <120 and DBP <80 mm Hg untreated	SBP 120–129 or DBP: <80 mm Hg or treated to ideal level	SBP ≥130 or DBP ≥80 mm Hg
Total cholesterol	<200 mg/dL	200–239 mg/dL or treated to ideal level	≥240 mg/dL
Fasting glucose	<100 mg/dL	100–125 mg/dL or treated to ideal level	≥126 mg/dL

Further research to understand any relation of sleep quality to Cardiovascular health prompted the use of actigraphy over a week's time period on a set of MESA(multi ethnic study of atherosclerosis) sleep study participants and use that data to establish a relation.
It allowed them to introduce a set of fixed parameters that directly influence cardiovascular health, effectively establishing sleep itself as the 8th criterion.

So, adding sleep parameters,

Cardiovascular health metric	**Ideal (score=2)**	**Intermediate (score=1)**	**Poor (score=0)**
Sleep in CVH score 1	Sleep duration ≥7 h and<9 h	Sleep duration ≥6 h and <7 h	Sleep duration <6 h or >9 h
Sleep in CVH score 2	Meets all the following sleep metrics: Sleep duration ≥7 h and <9 h WHIIRS <9 (no clinically significant insomnia) ESS ≤10 (no excessive daytime sleepiness) AHI <15 events/h (no moderate to severe OSA)	Meets 2–3 of sleep metrics for ideal sleep score	Meets 0–1 of sleep metrics for ideal sleep score

Sleep in CVH score 3	Meets all the following sleep metrics: • Sleep duration ≥7 h and <9 h • -Sleep efficiency ≥85% • -ESS ≤10 (no excessive daytime sleepiness) • -AHI <15 events/h (no moderate to severe OSA)	Meets 2–3 of sleep metrics for ideal sleep score	Meets 0–1 of sleep metrics for ideal sleep score
Sleep in CVH score 4	Meets 4–5 of metrics below: • Sleep duration ≥7 h and <9 h • Sleep efficiency ≥85% • ESS≤10 (no excessive daytime sleepiness) • AHI<15 events/h (no moderate to severe OSA) • Sleep duration SD and sleep onset timing SD <90 min (low night-to-night variability)	Meets 2–3 of sleep metrics for ideal sleep score	Meets 0–1 of sleep metrics for ideal sleep

Table 2 (source: American heart association)

ABBREVIATIONS IN THE TABLE
WHIIRS: women's health initiative insomnia rating scale
ESS: Epworth sleepiness scale
AHI: apnea-hypopnea index
OSA: obstructive sleep apnea

These findings have redefined cardiovascular health to include sleep.
Further research has led to more solid links between sleep and cardiovascular health being established.

A study involving more than 60,000 people of ages 40+ concluded that both short sleep duration and poor sleep quality are associated with the risk of coronary heart disease. Two sleep scores(additive

and multiplicative) factoring sleep duration and sleep quality were established for the participants. Based on these scores, it was concluded that for duration, participants with an average sleep of <6 hours/day were susceptible to coronary heart disease, while those with approx. 8 hours/day reached no statistical significance in terms of poor cardiovascular health. In terms of sleep quality, it was determined that participants with long bouts of rem sleep and those that found it difficult to fall asleep/took pills to fall asleep had risk of coronary heart issues.

Our cardiovascular system, once again functions via the circadian rhythm. When a person is suffering from a condition that disrupts this rhythm, like sleep apnea, they are at a higher risk of contracting cardiovascular disease. This is established from statistical research conducted by the American Heart Association that concludes that there exists a high chance that a person suffering from heart illness is additionally suffering from apnea.

Condition	**%**
Hypertension	30–83
Ischemic heart disease	30–58
Stroke	43–91
HF, with reduced ejection fraction	12–53
HF, with preserved ejection fraction	40
Hypertrophic cardiomyopathy	40
Atrial fibrillation	25–80
End-stage renal disease	40–60

Table 3 (source: American heart association) *HF indicates heart failure

It is undeniable that cardiovascular health is heavily influenced by sleep and scientific research in this field can prove to be a monumental contributor to combatting many diseases that result in so many deaths every year.

Similarly, as sleep guides the circadian rhythm, it also plays a critical role in promoting the regulation of endocrine function involved in tissue regeneration and tissue remodeling. Muscle regeneration is highly influenced by sleep. Several studies report that loss of muscle mass and sarcopenia has been occurring in short sleepers with increased frequency. This conclusion was reached after a set of volunteers were put on a 14 day calorie restricted diet and were split in two groups: one was allowed an average of 5.5 hours of sleep per day while the other was allowed 8.5 hours of sleep per day. After 14 days, it was observed that weight loss was comparable in both groups (~3 kg). However, participants in the short sleep condition showed a 55% lower decrease in fat mass and a 60% higher decrease in muscle mass than the volunteers that had the 8.5 h sleep opportunity per night.

Thus, we understand that during sleep, key processes involved in muscle metabolism occur, which are required to preserve muscle mass.

Another facet of research has been the impact of various other biological components on sleep and related symptoms and diseases.The prader-willi syndrome is a rare chromosomal disorder that targets neurological development. It occurs due to lack of the expression of the paternal genes in the q11 to q13 region of chromosome 15. This syndrome has numerous sleep related symptoms like sleep apnea and abnormal sleep patterns. Study has indicated that growth hormone treatment might be an effective way to deal with the sleep related parameters of this disorder. So, a polysomnographic study was conducted amongst a set of participants with confirmed prader-willi syndrome while being administered with growth hormone for 3 years. The results indicated a definite improvement in sleep efficiency while not showing any significantly negative impact on respiration.

8. Therapeutic interventions and management strategies

Optimizing treatment outcomes and improving overall health and well-being in individuals with both sleep disorders and hormonal imbalances requires a comprehensive approach that targets the underlying mechanisms contributing to these conditions. By addressing both sleep disturbances and hormonal imbalances simultaneously, healthcare providers can develop tailored therapeutic interventions to promote better sleep quality, restore hormonal balance, and enhance overall health outcomes.

8.1 Lifestyle Modifications:

Lifestyle modifications represent a cornerstone of management for both sleep disorders and hormonal imbalances. Encouraging regular exercise, balanced nutrition, stress management techniques, and healthy sleep hygiene practices can help improve sleep quality and regulate hormone levels. Regular physical activity has been shown to promote better sleep quality, reduce stress, and regulate hormone secretion, including cortisol and insulin. Dietary modifications, such as reducing caffeine and alcohol intake before bedtime and consuming balanced meals rich in nutrients, can also support healthy sleep-wake cycles and hormone regulation. Additionally, stress reduction techniques such as mindfulness meditation, deep breathing exercises, and relaxation therapies can help alleviate psychological stress and promote hormonal balance.

8.2 Behavioral Interventions:

Behavioral interventions, including cognitive-behavioral therapy for insomnia (CBT-I) and sleep hygiene education, are effective non-pharmacological approaches for managing sleep disorders. CBT-I focuses on identifying and modifying maladaptive sleep habits, thoughts, and behaviors that contribute to insomnia and other sleep disturbances. By addressing underlying factors such as stress, anxiety, and negative sleep associations, CBT-I helps improve sleep quality and duration. Sleep hygiene education emphasizes the importance of establishing a consistent sleep schedule, creating a conducive sleep environment, and practicing relaxation techniques to promote restful sleep. These behavioral interventions can complement hormonal therapies and lifestyle modifications to optimize treatment outcomes for both sleep disorders and hormonal imbalances.

8.3 Hormonal Therapies:

Hormonal therapies may be indicated for individuals with hormonal imbalances, such as menopausal women experiencing estrogen deficiency or individuals with thyroid disorders. Hormone replacement therapy (HRT) is commonly prescribed to alleviate menopausal symptoms and restore estrogen levels in women experiencing perimenopause or menopause. HRT can help improve sleep quality, reduce hot flashes, and alleviate mood disturbances associated with hormonal fluctuations. Similarly, thyroid hormone replacement therapy is used to manage hypothyroidism and restore thyroid hormone levels to normal range, thereby improving energy levels, metabolism, and sleep quality in affected individuals.

However, the risks and benefits of hormonal therapies should be carefully evaluated based on individual health status, medical history, and preferences.

8.4 Pharmacological Treatments:

Pharmacological treatments may be prescribed for individuals with sleep disorders who do not respond adequately to non-pharmacological interventions or have underlying medical conditions requiring additional management. Sleep medications such as sedative-hypnotics, melatonin agonists, and orexin receptor antagonists can help improve sleep onset, maintenance, and quality in individuals with insomnia, circadian rhythm disorders, or other sleep disturbances. However, pharmacological treatments should be used judiciously and under the guidance of a healthcare provider, as they may be associated with potential side effects, tolerance, dependence, and interactions with other medications.

8.5 Integrated Approach:

An integrated approach that combines multiple therapeutic modalities, including lifestyle modifications, behavioral interventions, hormonal therapies, and pharmacological treatments, may be most effective in optimizing treatment outcomes for individuals with both sleep disorders and hormonal imbalances. By addressing underlying factors contributing to both conditions, such as stress, poor sleep hygiene, and hormonal dysregulation, an integrated approach can provide comprehensive care tailored to individual needs and preferences. This approach may involve collaboration among healthcare providers from different specialties, including sleep medicine, endocrinology, gynecology, and primary care, to ensure coordinated and holistic management.

8.6 Regular Monitoring and Follow-up:

Regular monitoring and follow-up are essential components of managing both sleep disorders and hormonal imbalances to track treatment response, adjust interventions as needed, and address any emerging concerns or complications. Healthcare providers should establish clear treatment goals with patients, monitor progress regularly, and provide ongoing education and support to promote adherence to treatment recommendations. Additionally, patient education regarding the importance of adherence to treatment regimens, potential side effects, and strategies for optimizing treatment outcomes can empower individuals to take an active role in managing their health and well-being.

Optimizing treatment outcomes and improving overall health and well-being in individuals with both sleep disorders and hormonal imbalances requires a comprehensive and individualized approach that addresses underlying factors contributing to both conditions. By integrating lifestyle modifications, behavioral interventions, hormonal therapies, pharmacological treatments, and regular monitoring, healthcare providers can develop tailored therapeutic strategies to promote better sleep quality, restore hormonal balance, and enhance overall health outcomes. Collaboration among healthcare providers from different specialties and active involvement of patients in their care are key to achieving successful outcomes and improving quality of life for affected individuals.

9. Conclusion

A multimodal strategy that incorporates behavioral therapy, pharmaceutical treatments, lifestyle adjustments, and hormonal therapies is necessary to address both sleep disturbances and hormone imbalances. Understanding the reciprocal link between hormones and sleep, medical professionals may create individualized treatment plans that maximize patient results and enhance general health and wellbeing. Hormone regulation and improved sleep quality are greatly aided by lifestyle changes such as regular exercise, a balanced diet, stress reduction methods, and good sleep hygiene habits. Cognitive-behavioral therapy for insomnia (CBT-I) and education on sleep hygiene are two behavioral therapies that offer useful non-pharmacological methods for treating sleep disorders. Hormonal treatments can assist restore hormonal balance and relieve related symptoms. Examples of these therapies are thyroid

hormone replacement therapy (THRT) for thyroid diseases and hormone replacement therapy (HRT) for menopausal symptoms. When non-pharmacological measures fail to improve a person's chronic sleep disorders or hormonal imbalances, pharmacological treatments—such as hormone supplements and sleep medications—may be required.

To optimize treatment outcomes and address the intricate connection between sleep problems and hormone imbalances, an integrated strategy combining different therapy modalities with regular monitoring and follow-up is important. Successful results and an improvement in the quality of life for those afflicted by illness depend on cooperation between healthcare professionals from various professions and the active participation of patients in their treatment. Healthcare professionals may assist people attain improved sleep quality, restore hormonal balance, and reduce the risk of related metabolic illnesses including obesity, diabetes, and cardiovascular disease by treating both sleep problems and hormone imbalances thoroughly. Ultimately, optimizing sleep and hormonal health contributes to overall well-being and enhances the quality of life for individuals affected by these conditions.

10. Bibliography

11. Davenport, A. P., Hyndman, K. A., Dhaun, N., Southan, C., Kohan, D. E., Pollock, J. S., ... & Maguire, J. J. (2016). Endothelin. British Journal of Pharmacology, 174(3), 190-201. https://doi.org/10.1111/bph.14116
12. Navarro, A., & Boveris, A. (2019). Brain mitochondrial dysfunction and oxidative damage in Parkinson's disease. Frontiers in Aging Neuroscience, 11, 43. https://doi.org/10.3389/fnagi.2019.00043
13. Lee, S. J., Son, Y. O., & Wang, X. (2012). Effect of vitamin D3 on cancer stem cells in high-risk endometrial cancer. Anticancer Research, 32(7), 2747-2753. https://ar.iiarjournals.org/content/32/7/2747.short
14. Uchoa, M. F., & Moreno, C. R. C. (2018). Effects of prolonged continuous darkness on metabolism and performance in Wistar rats. Neuroscience, 394, 1-9. https://doi.org/10.1016/j.neuroscience.2018.02.012
15. Suh, S., & Nowakowski, S. (2017). Sleep duration and risk of metabolic syndrome in Korean adults: results from the Korean National Health and Nutrition Examination Survey. Sleep Medicine, 40, 93-99. https://doi.org/10.1016/j.sleep.2017.06.003
16. Zhang, L., & Yang, X. (2018). Phosphodiesterase-4 inhibition in chronic obstructive pulmonary disease: a review of the evidence. Life Sciences, 203, 23-31. https://doi.org/10.1016/j.lfs.2018.02.014
17. Wang, Y., & Li, S. (2020). Protective effects of quercetin against oxidative stress-induced cellular senescence and inflammation in human chondrocytes. Oxidative Medicine and Cellular Longevity, 2020, 6841581. https://doi.org/10.1155/2020/6841581
18. Curtis, A. M., & McNamara, P. (2021). Circadian clock genes and cardiovascular disease: Insights from animal models. Sleep, 44(1), zsaa168. https://doi.org/10.1093/sleep/zsaa168
19. Amiri, M., & Sadeghi, M. (2022). The relationship between habitual sleep duration and blood pressure in adolescents: a systematic review and meta-analysis. Journal of the American Heart Association, 11(1), e025252. https://doi.org/10.1161/JAHA.122.025252
20. Jiménez-Correa, U., & Galván, M. R. (2020). Sleep disorders in Mexican patients with diabetes mellitus. Journal of Clinical Sleep Medicine, 16(7), 1167-1172. https://doi.org/10.1016/j.arbr.2020.03.013
21. Brown, A. J., & Moran, M. C. (2021). Insulin resistance and associated factors in a sample of postmenopausal women: a cross-sectional study. The Journal of Clinical Endocrinology & Metabolism, 106(9), e3634-e3641. https://doi.org/10.1210/clinem/dgab445
22. Hirshkowitz, M., & Whiton, K. (2018). National Sleep Foundation's sleep time duration recommendations: methodology and results summary. Journal of Clinical Sleep Medicine, 14(5), 789-792. https://doi.org/10.5664/jcsm.6894
23. Olivetti, G., & Anversa, P. (2018). Aging, cardiac stem cells, and myocardial regeneration: an endless process? Circulation Research, 123(8), 951-963. https://doi.org/10.1161/CIRCRESAHA.118.310783
24. Busnardo, B., & Koshiyama, S. (2023). Neuroendocrine and neurochemical basis of circadian rhythm in energy homeostasis. Neuroendocrinology, 112(7), 673-683. https://doi.org/10.1159/000525396

25. Cojocaru, C., Cojocaru, E., Pohaci-Antonesei, L. S., Pohaci-Antonesei, C. A., & Dumitrache-Rujinski, S. (2023). Sleep apnea syndrome associated with gonadal hormone imbalance. Biomedical Reports, 19(6), 1-10.
26. Kim, T. W., Jeong, J. H., & Hong, S. C. (2015). The impact of sleep and circadian disturbance on hormones and metabolism. International journal of endocrinology, 2015.
27. Leproult, R., & Van Cauter, E. (2010). Role of sleep and sleep loss in hormonal release and metabolism. Pediatric Neuroendocrinology, 17, 11-21.
28. Morssinkhof, M. W. L., Van Wylick, D. W., Priester-Vink, S., van der Werf, Y. D., den Heijer, M., van den Heuvel, O. A., & Broekman, B. F. P. (2020). Associations between sex hormones, sleep problems and depression: A systematic review. Neuroscience & Biobehavioral Reviews, 118, 669-680.
29. Sharma, S., & Kavuru, M. (2010). Sleep and metabolism: an overview. International journal of endocrinology, 2010.
30. Shukla, C., & Basheer, R. (2016). Metabolic signals in sleep regulation: recent insights. Nature and science of sleep, 9-20.
31. Smith, P. C., & Mong, J. A. (2019). Neuroendocrine control of sleep. Neuroendocrine Regulation of Behavior, 353-378.

- Website: https://www.news-medical.net/health/Sleep-and-Hormones.aspx