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The Impact of Sleep Disorders on the Development of Metabolic Syndrome

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ABSTRACT

Sleep is an essential physiological function that influences metabolic regulation, endocrine balance, and cardiovascular health. This review examines the multifaceted relationships between various sleep disorders—including insomnia, obstructive sleep apnea, and circadian rhythm disturbances—and the development of metabolic syndrome (MetS). Drawing from epidemiological, clinical, and experimental studies, the article explores how disruptions in sleep quantity and quality contribute to insulin resistance, central obesity, hypertension, and dyslipidemia through neuroendocrine and inflammatory pathways. Particular emphasis is placed on the role of the hypothalamic-pituitary-adrenal (HPA) axis, melatonin secretion, and appetite-regulating hormones such as leptin and ghrelin. Furthermore, the bidirectional nature of the sleep-MetS relationship is discussed, including the impact of MetS on sleep architecture. The review also highlights the public health implications of rising sleep disorders in modern society, and outlines lifestyle, behavioral, and pharmacological interventions aimed at mitigating both sleep-related and metabolic risks. Future research directions are proposed to improve early diagnosis, prevention, and targeted treatment strategies for individuals affected by this comorbidity.

KEYWORDS: Sleep disorders; metabolic syndrome; circadian rhythm; insomnia; obstructive sleep apnea; insulin resistance; cortisol; leptin; type 2 diabetes; cardiovascular disease; sleep quality; HPA axis.

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INTRODUCTION

The current lifestyle is often defined by a 24/7 economy with inadequate rest and a continued stress burden. Sleep deprivation and fragmentation are known to be detrimental to metabolism. A lack of sleep is also measured by the extent of impairment of the ability to stay awake. Insufficient sleep has economic implications in terms of judgment errors and accidents. The importance of adequate sleep in cognition, reaction time, and mood is recognized (Sharma & Kavuru, 2010). Hormonal regulation of metabolism is critical during sleep; sleep restriction is known to lead to glucose intolerance, hyperphagia, and excessive weight gain. The overall evidence to date indicates that sleep mediates other behavioral factors affecting metabolism and contributes to metabolic health. (Katano et al., 2011). Coupled with other factors, sleep deficiency promotes weight gain and increases risk for metabolic syndrome and type 2 diabetes mellitus.

UNDERSTANDING SLEEP DISORDERS

Insomnia, obstructive sleep apnea, and periodic limb movement disorder are common sleep disorders. Insomnia is a persistent difficulty to fall asleep or stay asleep, leading to daytime dysfunctions. Insomnia is categorized as acute or chronic depending on its duration. Acute insomnia usually lasts for less than a month and is often caused by stressful life events, while chronic insomnia lasts for three or more months and is usually caused by psychological or physiophysiological factors. Chronic insomnia is frequently accompanied by psychiatric disorders such as depression or anxiety, which may independently increase the risk of metabolic syndrome. Over a period of time there is increased risk of high blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol levels. It leads to serious heart problems, diabetes, and stroke. Obstructive sleep apnea is a disorder in which breathing is interrupted during sleep. These episodes can last a few seconds to several minutes, occurring 5-30 times per hour or more frequently. It begins with a cessation of airflow for at least 10 seconds, accompanied by a decrease in blood oxygenation with an increase in heart rate and blood pressure, which may induce abnormality in glucose metabolism. Excess body weight is one of the main risk factors for development of obstructive sleep apnea, which thus becomes a common health problem with obesity. The risk of obstructive sleep apnea increases steeply with the severity of obesity. Polygraphic recording confirms the diagnosis of obstructive sleep apnea. These recordings simultaneously measure brain waves, abdomen and thoracic respiratory movements, oronasal airflow, blood oxygen saturation, and heart rate, while the patient sleeps overnight in the hospital or at home. Body Mass Index is widely used to assess body weight for height. Periodic limb movement disorder is characterized by recurrent stereotyped movements of the limb during sleep. The movements typically occur in clusters of 5-30 seconds apart and last for 10-30 minutes. Such movements disturb sleep and lead to excessive daytime sleepiness. This disorder is most frequently diagnosed in middle- to advanced-age men. Periodic limb movement disorder is associated with metabolic syndrome. There are two most common subtypes of metabolic syndrome. Several risk factors independently and additively contribute to metabolic syndrome.

2.1. Types of Sleep Disorders

According to the International Classification of Sleep Disorders, sleep disorders can be divided into six main groups: insomnia;

sleep-related breathing disorders; central disorders of hypersomnolence; circadian rhythm sleep–wake disorders (CRSWDs); parasomnias; and sleep-related movement disorders. Sleep disorders typically cause disturbances in the quality, amount, and timing of sleep, resulting in impaired daytime functioning and distress (B. J. Schipper et al., 2021).

Insomnia is the most prominent sleep disorder. Insomnia is characterized by dissatisfaction with sleep quantity and quality, often comprising difficulty falling asleep, maintaining sleep, waking too early, and/or non-restorative sleep. Insomnia is accompanied by distress or impaired daytime functioning and occurs despite adequate opportunity to sleep. Insomnia is more frequently reported by women and associated with heightened comorbid psychiatric disorders, including anxiety, depression, and posttraumatic stress disorder. Sleep-related breathing disorders' symptoms include loud snoring; observed episodes of breathing cessation during sleep; and excessive daytime sleepiness, fatigue, and/or insomnia. Central disorders of hypersomnolence: Excessive sleepiness during the day, recurrent periods of sleep or lapses into sleep, prolonged sleep episodes, and/or difficulty being fully awake. Circadian rhythm sleep–wake disorders: A persistent or recurrent pattern of sleep-wake disturbance that is primarily due to an alteration in the circadian system or in the sleep-wake cycle. Parasomnias: Abnormal behavioral or physiological events occurring during sleep and/or sleep-wake transitions.

2.2. Prevalence and Demographics

There is an increasing epidemic of sleep disorders among the adults and children population globally. With the pace of changing lifestyles, children and adults alike are being subjected to prolonged working hours and disrupted biological clock leading to increase in sleep disorders. Sleep studies have reported a rapid increase in the prevalence of sleep disorders in recent years. Obstructive sleep apnoea (OSA) has been reported to be the most common type of sleep disorders among them. Recent epidemiological studies have confirmed the association between sleep disorders and the development of metabolic syndrome (MetS). MetS is characterized by the clustering of 3 or more of the following: obesity (increased waist circumference), dyslipidemia (triglyceride level $\geq$ 150 mg/dl or HDL cholesterol $<$ 40 mg/dl in men and $<$ 50 mg/dl in women), hypertension (blood pressure $\geq$ 130/85 mm Hg or use of anti-hypertensive medication) and diabetes mellitus (fasting plasma glucose $\geq$ 100 mg/dl or impaired glucose tolerance) (Fan et al., 2020). Individuals who meet the criteria for MetS have a 2-3 fold risk of developing cardiovascular and cerebrovascular diseases than those who do not. Furthermore, MetS has emerged as a global pandemic affecting 35% of the adult population worldwide; thus, it is imperative to understand its risk factors for the prevention of the disease.

OSA is characterized by recurrent episodes of obstructed breathing with decreased arterial oxygen saturation during sleep. OSA has been reported to be associated with a 1.7-2.4 fold increased risk of developing MetS (Sabanayagam et al., 2012). The increased risk is primarily due to the chronic intermittent hypoxia that results in reduction in insulin sensitivity and increased body weight through activation of the hypothalamic-pituitary axis and increase in insulin level. Insulin resistance is one of the components of MetS. Long standing uncontrolled insulin resistance results in increased hyperinsulinemia leading to the deposition of triglycerides in the viscera and enlarged waist circumference, dyslipidemia and hypertension. There is also a bidirectional relationship between sleep disorders and metabolic syndrome. Individuals with MetS are at increased risk of developing sleep disorders.

2.3. Physiological Mechanisms

A multitude of pathways are known to mediate a myriad of effects of sleep deprivation or disturbance on metabolism, including the central nervous system, sympathoadrenal system, neuroendocrine system, glucose transport and metabolism, secretion of hormones, orexigenic or anorexigenic factors, inflammatory and cardiovascular factors, and enteric system (Hirotsu et al., 2015). Increasing evidence indicates that exogenous stressors increase the likelihood of sleep disorders in a vicious cycle. Stressors are influential agents that may provoke or amplify the severity of the disease process (Sharma & Kavuru, 2010). Perturbations in the endocrine environment, either directly through mechanistic pathways or indirectly via modulating behavior patterns, may yield profound and clinically significant pathophysiological effects, which also contribute to the development of SDBs in a positive feedback manner. The hypothalamic–pituitary–adrenal (HPA) axis is activated by stressors and is responsible for mediating various physiological changes, e.g. increased immunoreactivity for corticotrophin releasing hormone, increased secretion of adrenocorticotropic hormone from the pituitary gland, increased secretion of corticosteroid hormones from the adrenal glands, and increased modulation of neurons throughout several systems. Stress directly affects the activity of the sleep centers and sleep regulatory circuits. It has been demonstrated in rodents that exogenous acute restraint and swim stress affects sleep architecture via activation of HPA axis output. Stressors subsequently activate brain centers, including the PVN, ventrolateral preoptic nucleus, locus coeruleus, and tuberomammillary nucleus, setting into motion a cascade that affects sleep patterns. Chronic stressful experiences, including physical, psychological and social stressors, seem to also affect sleep in humans. The major effects of chronic stress on human sleep include increased sleep onset latencies; delayed sleep times; and decreased sleep efficiency and total sleep times.

OVERVIEW OF METABOLIC SYNDROME

Metabolic syndrome is a complex disorder characterized by central obesity, elevated blood pressure, dyslipidemia, and impaired blood glucose (Syauqy et al., 2019). Collectively, these components of metabolic syndrome elevate the risks of diabetes, cardiovascular diseases (CVD), and mortality, which enormously burden health systems. Individuals with metabolic syndrome tended to have increased levels of high-sensitivity C-reactive protein (hsCRP) and white blood cells (WBC), and might deteriorate the risks of metabolic diseases and CVD. Consequently, the interest of researchers and public health systems to address metabolic syndrome has significantly increased. The prevalence of metabolic syndrome has considerably increased in many countries. Central obesity was the underlying factor of metabolic syndrome, which was driven by excessive calorie intake and physical inactivity. Therefore, the identification of modifiable risk factors may be crucial to prevent the development of metabolic

syndrome. More than 50 years ago, the first prevalence study of metabolic syndrome was published. There is rapid growth in the literature on metabolic syndrome after the first definition was published. The identification of the insulin resistance syndrome since impaired glucose tolerance (IGT) was regarded as a cardinal feature of diabetic. More recently, sleep disorders have drawn increasing attention in relation to metabolic disorders. Short sleep duration has been reported to have negative effects on metabolic diseases such as obesity, hypertension, diabetes, and escalated mortality. Epidemiological studies conducted in various countries have consistently reported that short or long sleep duration was related to metabolic syndrome and its components as well as inflammation. Nevertheless, all of the studies discussed above have been performed in participations with varying metabolic syndrome statuses, including normal, borderline, and having metabolic syndrome not mentioned. In addition, it is noteworthy that the relationship between insomnia and metabolic syndrome remains unclear. That is, while some previous studies regarding this association in different populations demonstrated a positive relationship between insomnia and metabolic syndrome, some others did not demonstrate that. Thus, it is highly warranted to conduct a further study to clarify this association.

3.1. Definition and Criteria

Metabolic Syndrome (MetS) is defined by a cluster of risk factors for cardiovascular disease and Type 2 diabetes including central obesity, dyslipidemia, hypertension, and hyperglycemia (Syauqy et al., 2019). A person is considered having MetS when the waist circumference is ≥90 cm in men and ≥80 cm in women, plus any two of the following risk factors: systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or taking anti-hypertensive medication; triglyceride level ≥150 mg/dL or taking medications; HDL-cholesterol level <40 mg/dL in men or <50 mg/dL in women or taking medication; and fasting blood glucose ≥100 mg/dL or taking medications for diabetes (Katano et al., 2011). MetS is also known as a cardiometabolic syndrome, which is a cluster of risk factors of the cardiovascular diseases and Type 2 diabetes. It was first proposed by the World Health Organization in 1998 and is strongly related to obesity, high blood cholesterol, and sedentary lifestyle. It is now regarded as a global epidemic threatening human health and has become prevalent in both developed and developing countries.

3.2. Epidemiology and Risk Factors

Despite significant advances in our understanding of metabolic syndrome (MetS) and sleep disorders, the epidemiology of sleep disorders in MetS and its components is barely known (Hua et al., 2021). Knowledge of the mutual relationships between MetS and sleep disorders is limited at present. Moreover, healthy lifestyle behaviors are rarely examined in their association with both conditions simultaneously. This makes it difficult to differentiate the non-modifiable correlation from shared modifiable risk factors across the two disorders. Sleep plays an important role in cardiovascular and metabolic regulatory relationships that could shed light on their co-morbidity. Individuals with MetS components and sleep disorders have similar neuroendocrine alterations such as increased norepinephrine and cortisol levels and decreased heart rate variability which may reflect a similar patho-physiological disturbance. However, not all patients with sleep disorders have MetS or vice versa which suggests the existence of other risk factors.

Another perspective focuses on the unique input of each disorder. The adverse effects of sleep disorders on MetS and its components have been demonstrated in clinical and epidemiological studies. For instance, cumulative evidence supports the association between obstructive sleep apnea and increased body mass index, blood pressure, dyslipidemia, and hyperglycemia. A longitudinal study showed that controls of short sleep lead to decreases in waist circumference, systolic blood pressure, and fasting glucose. Alternatively, it also has been suggested that the chronicity and severity of MetS exacerbate sleep quality. Individuals with MetS components experience greater levels of sleep-disordered breathing events and greater daily oxygen desaturation. Strikingly co-morbidity of sleep disorders and MetS leads to higher severity of both disorders. Understanding the epidemiology and risk factors of sleep disorders specifically in MetS population may lead to the identification of new shared and unique risk factors underlying patient stratification, inform the design of intervention studies and promote awareness of their co-morbidities. This study aimed to summarize the evidence regarding the epidemiology of sleep disorders among MetS cohort studies and to reveal the existing knowledge gaps via critical synthesis.

3.3. Health Consequences

Obesity, type 2 diabetes mellitus (T2DM), and their cardiovascular consequences are pernicious conditions of ever-growing prevalence. The prevalence of obesity has doubled in the last 30 years in most countries; the numbers are growing most rapidly in developing countries. A recognized risk factor for metabolic syndrome is sleep disruption, a wide term encompassing all disturbances affecting sleep quality (Medic et al., 2017). Most of the research on sleep and metabolism has addressed the impact of sleep disruption on obesity, T2DM, and the metabolic factors that constitute them, including changes in appetite, body composition, fat distribution, insulin sensitivity, glucose control, and levels of metabolic hormones. It seems being awake during the night is pro-obesogenic, whereas sleep may be important for weight regulation.

Considerable attention has been given to health consequences that arise from sleep loss and sleep disorders, with a focus on sleep's impact on obesity and T2DM (Sharma & Kavuru, 2010). These diseases often serendipitously co-occur, and evidence is surfacing that they may mediate each other's effects. Here, an overview of the likely biological mechanisms through which sleep impacts energy metabolism and the development of obesity and T2DM is given. Sleep may be an appropriate treatment target for obesity and T2DM, controlling them alongside other targets with the potential to alter energy balance. Findings are based solely on observational studies of the impact of sleep disruption on population levels of BMI and T2DM or measures of homeostasis, with cross-sectional, case-control, prospective cohort, and experimental studies included. Metabolic causes of sleep disturbances are not considered. Sleep disruption leads to adverse changes in energy balance either through shifts in food intake or energy expenditure, which is especially clear for sleep loss, although food intake remains difficult to quantify. Notably, population sleep loss is unlikely to have led to a large rise in culture- and environment-level energy imbalance in humans.

Whereas the previous section was focused on his population, findings on the individual-level impact of sleep disruption on appetite and a schematization of its effects on key aspects of appetite regulation are presented. Much is known regarding these aspects, stemming from extensive published research on sleep deprivation's effects on appetite and its associated biological and behavioral pathways, although not all are necessarily pro-obesogenic. Together with effects on energy expenditure and glucose metabolism, alterations in appetite regulation provide a range of mechanisms through which sleep disruption may promote weight gain.

LINK BETWEEN SLEEP DISORDERS AND METABOLIC SYNDROME

The metabolic syndrome (MetS) is defined as the coexistence of metabolic risk factors that increase the risk of cardiovascular disease and type II diabetes. Although the definitions of MetS differ among organizations, most epidemiological studies utilize the definition proposed by the National Cholesterol Education Program Adult Treatment Panel III (Sabanayagam et al., 2012). Such studies have revealed that MetS is prevalent among Western countries and is becoming a major public health concern in Asia. However, the relationship between sleep disorders and the development of MetS remains unclear, especially in Asian countries. Therefore, the objective of the present study was to evaluate the association of sleep duration and insomnia symptoms with the components of MetS using the data of a physical examination cohort in Taiwan.

MetS is characterized by central obesity, elevated blood pressure, dyslipidemia, and impaired blood glucose. In 2005, the International Diabetes Federation proposed a new definition of MetS that was based on the NCEP ATP III definition and the World Health Organization definition. The definition used by the IDF was the same as that of the NCEP ATP III; however, it additionally stipulated that a waist circumference threshold was recommended instead of required for designation of central obesity. The diagnosis of central obesity is important since it raises the risk of the other components. MetS is associated with markers of inflammation, suggesting that chronic inflammation may be an underlying cause of MetS (Syauqy et al., 2019). However, the integrated effect of sleep disorders on the component status of MetS remains unclear. Most studies evaluating the relationship between sleep and MetS have focused on Western countries. The relevance of the findings to Asian countries is not clear. In Asian countries, sleep is considered to be more malleable than other lifestyle behaviors and can potentially lead to the prevention of MetS. Therefore, a population study in Asia was warranted.

4.1. Pathophysiological Connections

Sleep is essential for recovery of both physical and mental health. Sleep is an active physiological state of variable duration and quality, in which there is a natural inhibition of voluntary movement and reduced response to external stimuli. It is built through dynamic and proportioned cycles of different sleep stages. Sleep is not a passive state but an active physiological period of recovery of physical and mental health. Sleep is necessary for: (1) recovery of physiological function: cellular activity and metabolism; (2) maintenance of cardiovascular, respiratory and thermoregulation homeostasis; (3) enhancement of energy and metabolism; (4) development of resilience against daily stressors; (5) removal of waste and toxic materials that are deleterious to CNS function; (6) each behaviour associated with long-term potentiation of learning and memory is shaped by rapid eye movement sleep. Sleep quality refers to an individual's satisfaction with their sleep patterns is as significant as sleep duration in determining risks for various health problems.

Metabolic syndrome is defined by the presence of central obesity as determined by waist circumference, plus any two of the following five factors: raised triglycerides, reduced HDL cholesterol, raised blood pressure, raised fasting plasma glucose. The condition is linked to an increased risk of type 2 diabetes and cardiovascular disease. The condition is affecting an ever-growing numbers of people globally. Sleep is comprised of awake, rapid eye movement and non-REM sleep, which is subdivided into four stages based on electroencephalogram characteristics. Sleep is related to the neuroendocrine, metabolic and weight balance systems. Deprivation and an unbalanced sleep can cause significant metabolic alterations affecting issues such as obesity. In laboratory settings sleep restriction of four to five hours for about two weeks led to marked worsening of insulin sensitivity, excessive daytime sleepiness and hypertension endemic.

4.2. Influence of Sleep Quality

Investigating whether short sleep duration is associated with clustering of metabolic syndrome diagnostic components. Methods: Selected from the Takashima study, 1072 subjects predicted to be middle-aged or older, at least 40 years old, who had no history of hypertension, diabetes mellitus, hyperlipidemia, coronary heart disease or stroke were included in this study. Sleep surveys were conducted regarding average sleep duration. Cut-off values for sleep duration were set as follows: short (less than 6 hours), normal (6 to 8 hours), long (more than 8 hours). Data were collected on the following metabolic syndrome diagnostic components: dyslipidemia, hypertension, high fasting plasma glucose (FPG). Statistical analysis was performed using a multivariate logistic regression model to examine the aging-adjusted association between sleep duration and the clustering of metabolic syndrome diagnostic components. The equation of regression analysis is shown below. Results: 298 subjects (27.8%) satisfied the criteria of metabolic syndrome (MetS). 220 subjects (20.5%) reported short sleep duration, 573 subjects (54.1%) normal duration, and 279 subjects (25.9%) long duration. A significant association was found between short sleep duration and clustering of metabolic syndrome components after adjustment for age. The association remained significant after adjustment for engender age and HF diet (odds ratio 2.63). Conclusions: Obtaining sleep duration less than 6 hours was significantly associated with clustering of metabolic syndrome diagnostic components after adjusting for confounding factors such as age, gender, and lifestyle-related factors (Katano et al., 2011).

4.3. Role of Sleep Duration

Sleep duration is one of the most extensively studied sleep-related factors in relation to metabolic syndrome. Previous studies have reported that short and long sleep durations are associated with increased risks of metabolic syndrome and its components.

Another study reported that sleep duration was significantly associated with metabolic syndrome and all of its components based on a multi-country study among eligible participants in the Asia-Pacific region.

Sleep has been used as a covariate in many studies to assess the association between sleep disorders and metabolic syndrome. Although the underlying mechanisms are still largely unknown, sleep restriction has been purported to lead to metabolic dysfunction subsequently developing metabolic syndrome. Supported by experimental studies, it has been proposed that sleep deprivation leads to increased oxidative stress, inflammation, impaired glucose tolerance and insulin sensitivity, and sympathetic activation, which may subsequently lead to carotid intima-media thickness elevation in individuals with habitual sleep deprivation. Further, sleep extension improved metabolic functions of glucose regulation, blood pressure and sympathetic activation.

The findings indicate that cardiovascular and metabolic factors directly impacted by metabolic syndrome were more affected in participants without metabolic syndrome at baseline and insufficient sleep or prolonged sleep. In addition, monitoring of cardiometabolic factors other than metabolic syndrome was warranted in individuals with hours of sleep. Sleep satisfaction was confirmed to be directly and indirectly associated with improvements in metabolic syndrome through sleep-related variables. Comparing different age cohorts, a significant effect of sleep satisfaction and sleep duration was confirmed only in middle-aged participants.

CLINICAL EVIDENCE

The relationship between sleep and metabolism has seen a resurgence of interest in the last decade due to mounting evidence that sleep disorders can adversely impact metabolism and cause a multitude of weight-related disorders, including obesity, insulin resistance/type 2 diabetes, dyslipidemia, and the metabolic syndrome. More importantly, unlike other weight-related disorders, sleep disorders appear to be amenable to treatment with a variety of approaches including use of pharmacotherapy for insomnia or other sleep disorders, as well as behavioral approaches (Sharma & Kavuru, 2010). However, sleep disorders are widely under-recognized in clinical practice and thorough assessments of sleep are infrequently incorporated into the workup for the metabolic syndrome. The following sections of this review will summarize both the clinical and experimental evidence linking sleep disorders to the development of obesity, insulin resistance/type 2 diabetes, dyslipidemia, and the metabolic syndrome.

In the last several years, a growing body of clinical evidence has emerged which suggests that sleep duration is inversely associated with the prevalence of metabolic syndrome and its components among Japanese populations aged 35 years and older (Katano et al., 2011). These observations indicate that metabolic syndrome may be a potentially modifiable consequence of sleep duration. As the prevalence of short sleep duration appears to have increased in Japan in recent years, this may apply broadly to other countries as well. Longitudinal studies are needed to confirm or deny a causal relationship between sleep duration and metabolic syndrome. If sleep loss does cause metabolic syndrome, the potential for a public health intervention to mitigate the growing obesity epidemic is substantially increased. Sleep is already known to affect a variety of important public health issues, ranging from chronic disease processes, motor vehicle accidents, quality of life, and work productivity, among others.

5.1. Studies on Sleep Apnea

In the Framingham study population, the number of sleep hours per night was related to the risk of development of the MetS. Each 1-h decrease in sleep duration increased the risk of future MetS relative to adequate sleepers in men, but not in women. However, in the general US population, short sleep duration was consistently associated with higher odds of MetS among both non-obese and obese individuals. In the Multi-Ethnic Study of Atherosclerosis cohort, fewer than 6 h of sleep duration was significantly associated with a greater prevalence of MetS in general, and specifically with central obesity. In 189 older Brazilian domestic elderly, sleep duration ≤5 h was independently associated with a higher risk of MetS in women, but not men. However, existing literature regarding the possible association of self-reported sleep duration with the MetS is limited. Furthermore, prospective studies exploring the effect of sleep duration on MetS development are scarce.

Discovery of the biochemical pathways linking sleep and obesity has generated interest in sleep regulation of energy intake and expenditure. Potential mechanisms of this coupling vary widely. Sleep loss is associated with changes in hormones affecting appetite regulation and alterations in mood and cognition driving compensatory eating behavior (F. Drager et al., 2010). It has also been suggested that sleep loss is associated with alterations in glucose metabolism and insulin regulation which directly foster weight gain. Less temporal overlap of eating and sleep has been associated with increased weight. Sleep deprivation/obstructive sleep apnea respectively induce cardiovascular stress/inflammation on the basis of intermittent hypoxia, sleep fragmentation and sympathetic tone elevation. Persisting changes are widely postulated to induce atherosclerosis processes. Sleep also influences inflammatory processes, which may link to sleep in the acute form of common cold vulnerability. Further elucidation of these mechanisms should improve the understanding of the pathways linking sleep and the MetS and possibly suggest targets for future preventative and therapeutic interventions.

5.2. Research on Insomnia

Consequences of sleep deprivation and fragmentation are being increasingly recognized. Various urologic as well as other, non-urologic disorders exhibit a diurnal pattern. The molecular drivers governing this diurnal phenotype across multiple organs are just recently beginning to be elucidated. Metabolic syndrome itself, including its components such as obesity and altered metabolism, sleep pattern alteration, and urologic conditions such as nocturia and OAB all possibly exert effects on each other and thereby complicate one another. Longitudinal studies demonstrating sleep modulations to treat urologic conditions outcomes. Understanding the diurnal regulation of circadian metabolism and how it affects the onset of metabolic syndrome and its treatment is still in its infancy. Future studies will extract translational tools from the bench to the bedside to predict the onset of metabolic

syndrome and treat them.

We are a sleep deprived society with evidence showing that we sleep on an average 6.8 hours as opposed to 9 hours a century ago (Sharma & Kavuru, 2010). Around 30% of adults report sleeping less than 6 hours per night. The 24/7 economy and its subsequent impact on sleep patterns may be testing bodies limits to maintain metabolic and hormonal equilibrium. Prevalence of both diabetes and obesity has increased. Impact of sleep dysregulation on causing metabolic derangements is thus being increasingly recognized.

Many of the disrupted sleep may lead to obesity and diabetes, by impairing glucose tolerance and oxidative sensitivity, through altered GLP - 1, NE, sympathetic activity and Hr variability. Altered cortisol levels may explain some of these changes. Chronic short sleep duration has been shown to be associated with a greater worsening of metabolic syndrome and inflammatory markers. Both sleep and metabolic dysregulation are chronic & have cascading effects over years across individuals with some more susceptible than others. The sleep slow wave therapy (SST) exploration is still in its infancy, however still remains one of the most promising interventions as it is one of the few techniques that can augment and harness sleep to improve metabolic syndrome across disease states.

5.3. Impact of Restless Legs Syndrome

Restless legs syndrome (RLS) is a chronic neurosensorimotor disease characterized by an urge to move the legs which is usually accompanied by unpleasant or uncomfortable often painful sensations in the legs (Bener et al., 2019). RLS symptoms began or worsened on rest, were relieved by movement, and occurred in the evening or at night which were checked using a Guide Questionnaire. RLS is a burdensome sleep disorder characterized by the urge to move one or both legs, often accompanied by uncomfortable sensations in the legs. RLS affects 10%–15% of the general population and over 20% of primary care patients (Lindner et al., 2011). RLS can have profound negative effects on the quality of life and daily activities and is associated with significant economic, social, and healthcare burdens. The characteristics of the disease lead to poor sleep and daytime impairments. RLS has been significantly associated with diabetes, hypertension, obesity, and metabolic syndrome. Many studies provided evidence that sleep quality influences the glycemic control among patients with type 2 diabetes mellitus (T2DM) and approximately 37%–50% of patients with T2DM have sleep problems, which is higher than the general population. It is well known that there is an association between T2DM and quality of sleep. RLS and T2DM are both potentially debilitating diseases that must be treated, and against this background, this study suggests an effective screening tool for the quality of sleep related to glycemic index status among T2DM patients. There are some studies that sleep quality influences glycemic control among T2DM patients. It is reported up to 37%–50% of people with T2DM have sleep problems. There is a rise in the prevalence of T2DM in children and adolescents, and it is significant way to rectify the physiological presenting challenge. The treatment of RLS combined with T2DM is still a challenge because there is no evidence of screening tools for the quality of sleep involving T2DM and RLS.

PSYCHOLOGICAL FACTORS

Although there is still limited research on the psychological aspects of sleep disorders and the development of metabolic syndrome, some evidence suggests a significant role for psychological factors in this relationship. There is a growing body of research suggesting that sleep problems are associated with psychological disorders (Sharma & Kavuru, 2010). For example, anxiety has been strongly linked with both sleep problems and future risk of metabolic syndrome. Sleep deprivation has been reported to be associated with significant emotional changes and may be a precipitating factor for an episode of mania in those with bipolar disorder. Correlations between insomnia severity and anxiety and depression have also been reported, and more sleep-onset insomnia symptoms predicted later levels of anxiety and depression.

Other psychological symptoms or disorders assessed in the studies investigating the sleep disorder/metabolic syndrome relationship had mixed associations with the outcome. For example, a study reported a protective effect for a very wide definition of neuroticism, but other subtypes of neuroticism established in that study were found to increase the odds for metabolic syndrome. Symptoms of anger and hostility were also positively associated with metabolic syndrome in some studies but were not significantly associated with many of the other studies. This suggests that while a diagnosis of a psychological disorder may lead to an increased risk of metabolic syndrome, other aspects of psychological symptoms or features may provide important confounding or even protective effects.

Sleep problems may be a prodromal or early symptom of psychological disorders, which in turn may lead to increases in weight and risks for diabetes and cardiovascular diseases. Alternatively, the overall stress levels demonstrated by an increase in the cumulative number of sleep problems may affect hormone levels and metabolic function, leading to increases in weight and risk factors for metabolic syndrome (Hirotsu et al., 2015). OSA or other sleep disorders may be the primary cause of several of both future sleep problems and psychological symptoms and disorders.

6.1. Stress and Sleep Disorders

Stress is a physiological and/or psychological disruption factor that, when present, induces a certain degree of tissue injury. In animals, it is believed that in response to external pressure, the amiable environment is disturbed; therefore, defense mechanisms are activated and activate an internal environment to attempt returning to predictable conditions. The most well-known consequence of chronic and/or intense stress is the emergence of glucocorticoids, a group of steroid hormones synthesized in the adrenal cortex, which, among other things, provoke an increase in blood glucose levels. Dysfunction of the hypothalamus–pituitary–adrenal (HPA) axis is believed to be involved in stress-related sleep disorders such as insomnia and obstructive sleep apnea (Hirotsu et al., 2015).

Sleep disorders are also considered a chronic stressor and have been linked with metabolic syndrome (MS). Sleep is a process that is believed to be as vital as feeding, thirst, and mating behaviours. Sleep is classically divided into the non-rapid eye movement (NREM) stage and rapid eye movement (REM) sleep in mammals. Sleep is in constant control by both endogenous and exogenous factors. Sleep timing is actively reinforced by a timing mechanism synchronised by the light–dark cycle. In adulthood, sleep loss and/or excessive sleepiness are believed to impair metabolic functions, predisposing to some degree of metabolic dysfunction (Sharma & Kavuru, 2010).

6.2. Anxiety, Depression, and Metabolic Health

The regulation of the HPA axis and, consequently, the synthesis and release of glucocorticoids, are controlled by multiple inputs from different CNS regions and projection systems. Acute or mild stressors transiently activate the HPA axis and enhance the secretion of glucocorticoids with antioxidant properties that counteract excess oxidative stress. Thus, it is assumed that the HPA axis minimizes the likely physiological impact of stress on brain function and metabolic processes through the acute release of glucocorticoids. In rodents, prolonged psychological stress leads to HPA axis hyperactivity. A chronic inflammatory environment and metabolic dysfunction that in turn lead to insulin resistance, are induced by elevated glucocorticoid levels and/or hypersecretion of cytokines characterized by the increased levels of pro-inflammatory interleukin in brain areas involved in energy balance and mood regulation.

Bidirectionally, chronic stress poses a risk for both the development and exacerbation of several metabolic disorders. This offers some insight into the roles that the actions of neuropeptides and the chronic stress-induced increase of several stress hormones play in the metabolic disturbances observed in stress-sensitive disorders. Clinical data link chronic stress with metabolic disturbances, including obesity, chronic inflammation, dyslipidemia, and insulin resistance, thus forming the basis of the pathophysiological concept of MetS. Stress has been proposed as a trigger for the onset or deleterious progression of risk factors for cardiovascular disease, such as MetS. The last decades of pre-clinical research aimed at elucidating the physiological and biochemical processes underlying the pathophysiological effects of acute and chronic stress, have produced considerable advances in this regard. Today, much is understood about how the stress-related activation of hormones and neuropeptides gives rise to trans-synaptic and extra-synaptic changes in the balance of several equally important mediators of biological rhythms, energy metabolism, inflammatory processes, and mood regulation.

In this respect, many different variations in the hypothalamus, including the NTS, are found. Nevertheless, it should be noted that it is difficult to disentangle the contribution of the sleep disorders themselves from the co-morbid depression and/or anxiety symptoms on metabolic health outcomes. Sleep is considered a global physiological state that alters neurocognitive functioning, and its quality is influenced by many physiological systems. Such systems include the glucose metabolism, which is central to several metabolic disorders, including prediabetes, T2DM, and MetS. Sleep quality is important to consider as a risk factor in these metabolic disorders, and recent work has shown a significant association between sleep quality and neurocognitive functioning in the MetS context. Further investigation on the direct neural and physiological routes between sleep quality, neurocognition, and metabolic health is needed to clarify their interrelationship.

LIFESTYLE AND BEHAVIORAL INTERVENTIONS

Several lifestyle and behavioral changes may improve sleep and lower the risk of metabolic dysfunction. Obtaining enough physical activity on a regular basis is key in managing both sleep and metabolic health. Cross-sectional analyses indicate that greater levels of moderate-to-vigorous physical activity are related to lower levels of metabolic syndrome, while greater amounts of sedentary time are associated with a higher prevalence of metabolic syndrome. In some full-scale intervention studies, increasing levels of physical activity, regardless of type, consistently led to improvements in sleep quality (Chaput et al., 2022). Furthermore, exercise may reduce blood glucose in those with type 2 diabetes and promote circadian re-entrainment. In particular, morning exercise may help enhance metabolic health, sleep health, and mental health during travel across time zones.

Healthy eating patterns are another useful behavior for promoting both optimal sleep and metabolic health. Diets consistent with established recommendations have a well-documented inverse association with metabolic syndrome risk. Eating an unhealthier diet appears to increase its incidence. In terms of sleep, certain diets are positively associated with sleep quality, while others are related to lower sleep quality. Experimental studies suggest that increased fruit, vegetable, whole grain, fish, and lower sugar sweetened beverage intake may uniquely reduce sleep onset latency, insomnia risk, and poor sleep quality, likely owing to their anti-inflammatory effects. Thus, if desired, working toward eating more like a Mediterranean diet may be a good approach for improving both sleep and metabolic health.

Proper management of light exposure across the day may also be beneficial for sleep and metabolic functioning. In an observational study that used self-reported measures of light exposures, greater bright daytime light and dim evening light exposure appeared to be important for circadian alignment and benefited metabolic functioning on both leisure and workdays. Using light boxes and obtaining bright light exposures in the morning could help advance circadian timing in those with delayed timing, such as night shift workers. On the other hand, preventing excessive evening exposures to bright indoor light, especially from digital devices, can also help address circadian timing disorders. Short naps of up to about 40 minutes or so have been shown to have health benefits, but longer naps may increase the risk of metabolic syndrome and impair health outcomes. Consuming caffeine late in the day is well known to disrupt sleep quality and could further contribute to circadian timing issues. Alcohol consumption is recommended to be on the lower side. Smoking may also be harmful for promoting healthy sleep and metabolic regulation. As such, adopting these healthy lifestyle behaviors is possibly an important step in addressing the major public health issues of sleep problems and metabolic disorders, as well as engaging in effective treatment strategies for such sleep problems and/or circadian disorders.

7.1. Sleep Hygiene Practices

Sleep hygiene refers to the routines and environmental factors that influence sleep quality. Improving sleep hygiene can help promote sleep and treat some sleep disorders. Sleep hygiene interventions provide education about the following sleep hygiene practices: avoid racing thoughts, worry, excitement, and scary images before bedtime; arranging the bedroom to be as dark, quiet, and cool as possible; going to bed and waking up at the same time every day; getting out of bed if not asleep after 15 minutes; limiting naps; avoiding caffeine, nicotine, and alcohol before bedtime; to not exercise vigorously too soon before bedtime; and getting bright light exposure in the morning and dim light exposure in the evening (Chaput et al., 2022). Sleep hygiene alone is often insufficient to address sleep disorders among older adults, as pharmacological interventions may be necessary. Further, few studies have formally evaluated the efficacy of sleep hygiene interventions among older adults.

Some sleep hygiene practices may be less acceptable to some groups of people. Furthermore, certain groups of people, such as those with greater cognitive impairment, may not use some sleep hygiene practices effectively. Interventions targeting the user-friendly side of sleep hygiene may include information to paint a clear picture of the pre-sleep situation when insomnia is prevalent. Some methods, such as asking an individual about their personal sleep hygiene practices, may be more effective than showing them general information (A. Chaudhry et al., 2023). Other methods, such as using smartphone-based sleep hygiene apps that provide video scenes of bedtime situations, post a complex picture of sleep hygiene practices with potential suitable ways.

7.2. Dietary Modifications

The human diet has significantly changed in the past century; for example, greater amounts of sugar and fat-laden processed foods have been added to dietary patterns, which may present an unrecognized problem related to sleep and circadian health (Chaput et al., 2022). Nutrition is intricately connected to sleep and circadian timing. Some dietary components can impair sleep and circadian rhythms, while others can promote greater balance. Thus, strategies for improving dietary behaviors and food patterns may be considered in tandem with approaches to improve sleep and circadian health. Prioritized consumption of whole and minimally processed foods may help to bolster sleep and circadian health. Increasing the number of meals and snacks based on whole foods may promote a more circadian-neutral diet than periodic overeating that is commonly observed among individuals with night eating syndrome and guilt-cycles of binge eating. Encouragement of better food environments may provide access to healthier foods and alleviate various domains of ethos, culture, and biodiversity that common, but less healthy, staple foods fail to encompass.

Emerging data suggest that diet, sleep, and circadian health may also independently influence health behaviors and mental wellbeing among adolescents. Simply restraining a diet can impair metabolic health if food timing is inadequate. Strong adherence to a high quality, continental-style time-restricted diet is protectively associated with good sleep. Promotion of healthier fatigue or deprivation recovery strategies has the potential to help alleviate side effects of sleep and circadian related disorders and contribute to healthier dietary patterns. Partnerships with food service and built environment organizations may improve dietary quality. Attention by the public health community to improve food patterns, along with sleep and circadian health, may provide an avenue for improving the wellbeing of vulnerable populations.

7.3. Exercise and Physical Activity

Increased afternoon and evening physical activity is well known to be associated with lower levels of metabolic syndrome, however, it appears that there are subtle trade-offs that relate to sleep indices and physical activity timing. The findings support recent evidence showing a synergistic health effect of weekend physical inactivity and acute excessive sleep on the development of metabolic syndrome and increased mortality (Chaput et al., 2022). Nonetheless, those who are regularly physically inactive may remain at elevated risk for metabolic syndrome even if they sleep for extended periods on the weekends. Some what unexpectedly, night-time physical activity was not significantly associated with metabolic syndrome overall. However, it was found that those who participated in excessive night physical activity and sufficient sleep were at increased risk for metabolic syndrome. This suggests that evening physical activity should be strongly discouraged owing to a disturbance of night-time sleep; however, it is likely that the effect on health is somewhat small. Limitations in this area of research include a reliance on actigraphy information, when diary or calendar information might provide expanded context, and other sleep indices such as sleep duration that were not studied but may have important implications. This study found a strong cross-sectional association between day-by-day changes in physical activity, sleep duration, and metabolic syndrome. Whether being physically active helps to prevent or reduce the metabolic health consequences of insufficient sleep and circadian misalignment, when both sleep and METS were measured live, is currently unknown. Evening physical activity was found to be related to metabolic syndrome across all participants, more so among those who slept well, or with less than 60 minutes buffered nocturnal sleep. Late-night physical activity may be detrimental to metabolic health, a sector of physical activity generally not aligned with a circadian approach to health that may be at risk of excessive sedentary health behaviour and eventually metabolic syndrome most. These findings are relevant to future cross-sectional studies linking fully continuous actigraphy measures or other modern day sleep epochs and daylight estimating parameters to metabolic syndrome indices.

PHARMACOLOGICAL APPROACHES

For metabolic disease, lifestyle changes focusing on dietary quality, physical activity, and sleep habits can serve as a first-line treatment but are often unsuccessful clinically due to poor compliance. Adverse behavioral and environmental factors such as nutrient deficiency, obesity, excessive alcohol, drug abuse, high stress, and sleep disruption impair metabolic homeostasis, leading to gestational diabetes, diabetes, metabolic syndrome, obesity, gout, hyperlipidemia, chronic hepatitis, fatty liver, and consequently, heart disease, stroke, renal failure, and cancer (Nohara et al., 2015). A growing body of evidence suggests that metabolic disease development is influenced by circadian and sleep disruption. Therefore, it is also important to develop pharmacological agents, which normally do not require drastic and prolonged lifestyle modification and thus promise greater

patient motivation.

Melatonin is secreted in a circadian-dependent manner and helps maintain visceral adipose mass and expected metabolic profiles. Human studies have provided association evidence supporting a direct relationship between melatonin levels and the risk of developing type 2 diabetes. Temporally misaligned food intake leads to alterations in the endocrine environment that promotes metabolic disease. Various pharmacological approaches have been attempted to rescue the disruption of metabolic homeostasis caused by misalignment of behavior and the internal clock. Although the elimination of phosphorylated kinases in the hypothalamus and/or ablation of melatonin membrane receptors effectively ameliorated metabolic dysregulation, a common downside is that these approaches blunt circadian/diurnal expression, thereby either directly or indirectly impairing multiple physiological pathways.

8.1. Medications for Sleep Disorders

Pharmacologic treatments for sleep disorders in patients with metabolic syndrome have multiple options. It is important to note that the relationship between the medications and metabolic syndrome is often complicated, and for some medications with favorable effects on sleep, adverse metabolic consequences may be expected. Therefore, the selection of the agent should consider the potential impact on both sleep disturbance and metabolic risk factors (Sharma & Kavuru, 2010).

8.1.1. Melatonin/Agonists of Melatonin Receptors Traditionally used for treating circadian rhythm sleep disorders, exogenous melatonin has been noted to have inhibitory effects on metabolic syndrome-related insulin resistance, inflammation, and oxidative stress. Agonists of melatonin receptors such as ramelteon and tasimelteon, approved for insomnia and circadian rhythm sleep disorders respectively, are less well studied in metabolic syndrome than melatonin itself. The current evidence on both melatonin and agonists of melatonin receptors regarding treatment of sleep disorders is limited.

8.1.2. Benzodiazepine Receptor Agonists Known for their anxiolytic and hypnotic properties, they have been shown to improve sleep efficiency in patients with concomitant metabolic syndrome. However, medication-related weight gain and the reversal of physiological effects on sleep by an abrupt withdrawal of medications can be major concerns when using the agent in this population. Obesity/hyperphagia-promoting effects have been particularly noted for triazolam and zolpidem. Long-half-life medications such as estazolam and zaleplon that likely improve sleep without early rebound effects can be considered alternatives.

8.1.3. Antipsychotics Even though they are mainly used for treating psychosis/schizophrenia, the atypical antipsychotics, such as quetiapine and olanzapine, have been used off-label for primary sleep disorders as well as comorbid mood/anxiety disorders on the premise that an improved mood and reduced anxiety would lead to better sleep. Sleep-laboratory studies of quetiapine, olanzapine, and clozapine among other medications have revealed increased total sleep time and improvements in sleep maintenance. However, this class of medications is also well-known for causing weight gain, dyslipidemia, glucose intolerance, and frank diabetes mellitus.

8.2. Impact of Pharmacotherapy on Metabolic Syndrome

Excessive sleepiness is prevalent in metabolic syndrome, and a hypothesis is proposed that an imbalance of sleep drive in favor of wakefulness may increase the risk of metabolic syndrome. The acute impact of pharmacotherapy with nonselective noradrenergic, dopamine, and histaminergic dual action compounds on the sleep–wake cycle and levels of appetite-related hormones in patients with metabolic syndrome is investigated. The sleeping time between the groups does not differ significantly; however, at baseline, few individuals with metabolic syndrome were hyperinsomniac compared with controls. The pharmacological intervention group manifested a significant decrease in sleepiness when compared with the placebo group, and the decrease was significant for both medications in paired comparisons. Anxiety symptoms decrease more in patients with metabolic syndrome on armodafinil than on placebo. Metabolic syndrome elevated obesity, dyslipidemia, prolonged sleep latency, sleep inefficiency, sleep disturbance, and insomnia severity. Control displays higher obesity, waist circumference, sleepiness, depression, and arousal than healthy individuals. Sleep duration is unassociated with metabolic syndrome (Sharma & Kavuru, 2010). For middle-aged and older adults, metabolic syndrome is more common in those who are older, have more education, have a lower amount of sleep, or have more severe insomnia symptoms. In multiple linear regression, sleep duration and insomnia symptoms affect metabolic syndrome risk. Good sleep hygiene is beneficial to reduce metabolic syndrome risk factors (Syauqy et al., 2019). In general, for Taiwanese middle-aged and older adults with metabolic syndrome, insomnia symptoms, and sleep duration might be linked with abdominal obesity, hypertension, and fasting blood glucose levels; otherwise, they are associated with triglyceride levels in some subgroups.

FUTURE RESEARCH DIRECTIONS

Despite a growing awareness of the bidirectional interplay between sleep and metabolic homeostasis, the research in this burgeoning field is in its infancy. Most studies examined the “individual” influence of sleep on energy metabolic measures in populations with preexisting cardiovascular disease risk factors. Built on evidence of circadian rhythm dysregulation contributing to the pandemic of metabolic syndrome (Sharma & Kavuru, 2010), emerging research has begun to explore the role of disrupted sleep patterns secondary to light exposure during night-time hours on glucose homeostasis and metabolic health in healthy young adults. Highlighting a novel area with substantial translational implications, this systematic review aims to examine the prevalence, impact, and biological underpinnings of disrupted sleep cycles secondary to artificial night-time light exposure on glucose metabolism in young adult study populations. A literature review of studies assessing light at night exposure and glucose metabolism among healthy young adults aged 18-40 years was performed. Eligible studies were abstracted by two independent authors according to specific criteria concerning the presence of relevant exposures and outcomes. The association of disrupted sleep cycles secondary to light at night on glucose metabolism was supported by data from six individual studies with varying sample sizes, methodologies, outcomes, and effect sizes. Owing to the affordability and accessibility of light-emitting-diode-based lighting systems for 24/7 commercial and leisure activities, nighttime urbanization has exponentially increased globally (A. Chaudhry et al., 2023). Strong evidence suggests that nighttime urbanization and accompanying exposure to artificial light at

night negatively influence human health, including the risk of obesity and metabolic dysregulation. Building circadian rhythms primarily via exposure to light, sleep, and metabolic cognition are indeed interconnected. Despite a surge in research investigating metabolic disturbances from disrupted sleep-wake cycles, there exists limited literature that specifically examine disrupted sleep due to light at night exposure and its influence on metabolic health in young adults (aged 18-40 years).

9.1. Longitudinal Studies

Various longitudinal studies have reported the association between sleep duration and metabolic syndrome (MetS). A systematic review and dose-response meta-analysis aimed to explore the association between sleep duration and metabolic syndrome risk in adults, with findings indicating that both short and long sleep duration are significantly associated with increased risk of MetS. Suspecting of pooled estimates showed that the significant dose-response relationship existed in Asian cohorts, but not in American cohorts (Hua et al., 2021). Based on BMI changes in adults from childhood, the participants were categorized into 3 groups as follows: persistent normal weight, persistently overweight, and late overweight, with obesity risk analysis in individuals aged > 18 years with follow-up BMI $\geq$ 25.0 kg/m^2 at the last survey.

To test the association between sleep duration at each life stage and risk of overweight/obesity, weighted multivariate logistic regression to estimate relative odds ratios were used. Adults with late overweight were significantly associated with increased odds of short sleep duration at age 8, age 12, and age 16 years. In middle-aged and older adults with persistent overweight, participants with short sleep duration at age 8 were also significantly associated with higher odds of risk of overweight/obesity. Late overweight individuals were significantly associated with short sleep duration at age 8, age 12, and age 60 years. Persistent normal weight individuals were significantly associated with 2 metrics of long sleep duration in 2000 and 2006.

In a cohort of 6474 adults free of diabetes with valid data on baseline sleep duration and adjustment for a wide array of confounders, weight gain over 6 years significantly predicted the development of diabetes. These results suggest that weight gain is a precursor of future diabetes, prompting a ‘pre-diabetic’ status. Frequent SDB indicates an increased risk of type 2 diabetes mellitus independent of BMI. Given the cross-sectional nature of baseline data, the results are consistent with others. It is considered that they may be useful for guiding future studies of longitudinal, multi-ethnic cohorts of primary care settings in assessing the potential benefits of effective SDB treatment.

9.2. Intervention Trials

Intervention studies on the influence of sleep quality on metabolic syndrome and its main components are currently scarce. A search of the literature from 2009 to 2019 using the keywords “sleep intervention” and “metabolic syndrome” found only 36 results. A review of these articles indicated that the focus of most studies was on sleep apnea, four studies on sleep deprivation, and three studies on circadian rhythm disturbances. Thus, only six studies focused on sleep quality. In addition, half of the studies conducted a lifestyle intervention. Sleep studies mainly adopted subjective measurement tools, although objective measurements have been shown to be more reliable. Studies that examined predictors of metabolic syndrome have approached it from different angles, which also complicates comparisons among studies. A recent meta-analysis indicated that sleep quality and metabolic syndrome have a bidimensional association, but there have been no mediation studies (García-Serrano et al., 2022). The existing intervention studies mainly approached sleep quality from a SG improvement focused mainly on middle-aged participants with sleep complaints and few from a lifestyle perspective, these being more scarce with participants from Eastern cultures. Overall, the literature suggests that greater sleep quality improvement is needed, and as a broader takeaway, that it is possible to address metabolic syndrome in a holistic manner through sleep education and lifestyle improvements involving daily routines and behaviours.

Regarding weight and central obesity reduction, the studied factors did not mediate the impact of sleep quality. As pointed out in a recent review, the relationship between sleep quality and obesity is bidirectional – poor sleep quality predisposes to obesity and vice versa. Other physiological factors should be taken into account. Participants in this study were relatively young and were healthier than in other studies that suggested a significant impact on weight and central obesity. Furthermore, other studies have presented a significant portion of participants with sleep disturbance complaints, while this study specifically selected healthy participants. As this study aimed to explore the impact of sleep quality independently, associations between weight and sleep quality were examined using subjective measurements. A bidirectional correlation between weight and sleep quality was revealed through objective measurements. Nevertheless, there was a clear improvement in overall health and metabolic- and weight-related health markers.

The role of sleep in the development of obesity and the metabolic syndrome has wider public health implications. With the advent of workstation based societies, light at night exposure, a hectic schedule with an increased reliance on technology and electronic media, the average sleep duration has significantly declined. Evidence suggests that humans are sleeping on an average of 6.8 hours per night as compared to 9 hours per night a century ago. Prolonged sleep deprivation and subsequent metabolic derangement can pose significant public health challenges as sleep disorders can be potentially remedied or prevented in a society. Macro- and micro-economic loss due to conditions caused or exacerbated by sleep disorders has been estimated to be approximately 900 billion dollars per year. Non-drug, safer and more long-lasting interventions and options are also available. As sleep is modifiable, a targeted focus on sleep may lessen the burden of non-communicable diseases and their complications and improve the macro-economy. In order to successfully implement this, the barriers to its implementation must be identified and addressed. An awareness of the public health implications of sleep disorders is paramount because of the relevance of sleep to the public's general well-being and development. Sleep disorders have widespread public health implications. With fast-paced lifestyles of the 21st century, long travel and commuting times, and the increasing use of multimedia entertainment systems late into the night, sleep and its quality have become more compromised than at any other time in human history. With the exponential

rise of smart devices, like cell-phones, sleep hygiene has been significantly compromised globally; light at night exposure from electronics has especially had its impact on sleep and circadian rhythm. With these profound changes in lifestyle taking place, more than half of the adult population report inadequate sleep and more than one quarter of the adults report insomnia symptoms (Sharma & Kavuru, 2010). It has also been previously established that sleep and obesity are interconnected, as there are a variety of both behavioral and biological factors that play a role.

10.1. Awareness and Education

The recognition of sleep as a vital component of health is an important prerequisite for making progress in the treatment and prevention of sleep disorders. A number of initiatives in various cities and communities have reported to be effective in providing awareness education, support and help regarding sleep and its disorders. These are collectively termed as 'Sleepless Cities'. Major governmental initiatives have been made by many countries outside India also to recognize sleep related issues and affect policy and practice across various disciplines including pedagogical, manufacturing and health. Similar discussions and actions to mobilize support and funding agencies are needed in India and also desired throughout the world with special efforts in developing countries.

Effects of sleep deprivation and/or fragmentation are being increasingly recognized in humans. Societies are sleeping less. NASA space shuttles astronauts have recorded progressively reduced hours of sleep. A century ago, people in the United States actually spent 9 hours in bed; now they average only about 6.8 hours. One in five older adults, one-third of schoolchildren, and 30% of adults report sleeping less than 6 hours a night, these statistics are underreported as some adults may not be aware of their wakefulness during nighttime or do not report fragmented sleep to healthcare providers. Other segments of the population including the sick and unable to sleep well or who work in shift, two or three jobs to make ends meet may face a graver problem. Employers in many industries and occupations have difficulty hiring sufficient dedicated and alert workers due to competing demands on their time.

The 24/7 economy and its subsequent impact on sleep patterns and disruption of circadian rhythms are testing the bodies limits to maintain metabolic and hormonal equilibrium. Metabolic syndrome and its individual components are common and increasing problems. Worldwide prevalence of obesity has tripled since 1975; in 2022, WHO estimates that globally 1.9 billion adults, 18 years and older, were obese. Worldwide prevalence of diabetes has increased from 108 million in 1980 to 422 million in 2014. Updating progress made by the scientific community in understanding the impact of sleep dysregulation on causing metabolic derangements are important as both sleep and metabolic dysregulation are common and growing problems (Sharma & Kavuru, 2010).

10.2. Policy Recommendations

Given the results of the present study and understanding of the modifiable risk factor nature of sleep, policy recommendations for the public health field are put forth. Education and outreach initiatives regarding healthy lifestyle habits for emerging adults are waning. Much recent emphasis is on promoting positive eating and physical activity habits in local newspapers, social media, schools, and workplaces. However, many of the national initiatives promoting healthy lifestyle habits amongst the general public either omit sleep and sleep-related behaviors or marginalize their role as a risk factor for metabolic syndrome (MS) risk and severity.

Policy and outreach options should reference the literature supporting the relationship between sleep and health, including but not limited to cardiovascular disease, diabetes, hypertension, obesity, and MS risk and severity (A. Chaudhry et al., 2023). Furthermore, promoting sleep hygiene techniques with accompanying rationale, such as limiting caffeine intake within 6 h of sleep onset and maintaining a regular sleep schedule on weekdays and weekends with ≤1 h of variability, is paramount for emerging adults to understand how their decisions, such as staying up late to socialize or study, are influencing and putting their long-term health at risk (Chaput et al., 2022). Gatherings in different settings, including on-campus large events, student-led organizations, and social gatherings at bars or social settings, should add discussion of sleep and its relationship to metabolic health and other lifestyle habits to their programming and outreach initiatives. This outreach should be geared towards both the young adult guests and adult promoters of these events, as a stricter enforcement of healthy festivities will likely yield better outcomes.

Developing promotional and outreach materials addressing lifestyle habits should encompass sleep and sleep-related behaviors as strongly as they do promoting exercise and portability of healthy beverages and foods. Further, outreach initiatives should ideally be fully collaborative amongst outreach groups to better promote healthy choices across multiple domains (i.e., sleep vs. diet and activity). Policymakers and scientists are currently assessing the impact of k-12 school start times on sleep duration, sleep health, and health outcomes in preadolescents and adolescents. In the wake of the shifts towards later school start times, the adolescent-bias for later bedtimes and short sleep duration would still require momentum in emerging adulthood to ensure longer sleep and more optimal health, fully maximizing benefit from policy efforts.

CONCLUSION

Sleep is an important physiological function that promotes homeostasis and health. The sleep/wake cycle profoundly influences hormone production, metabolism, and activity of several organ systems (Sharma & Kavuru, 2010). Excessive metabolic demands resulted in the evolution of sleep and circadian rhythms in most organisms on this planet. Disruption of sleep schedules and attenuated sleep quality has been linked to metabolic disturbances, including obesity, diabetes, hyperlipidemia, and hypertension. Metabolic syndrome (MetS) is defined as a specific aggregation of metabolic risk factors that increases the risk for cardiovascular disease and type 2 diabetes. The risks associated with disturbed sleep and MetS warrant a comprehensive review of translations

in this relatively new field of study.

Contemporary understanding of sleep physiology and circadian rhythms stems from the study of sleep disorders. Sleep disorders form a major focus of clinical and bench research endeavors, and insights gained in this field have led to a peer-reviewed explosion of published work on the basic biology, evolution, and neurophysiology of sleep. Advances in biochemical and cellular manipulation methods continue to reveal more about the fundamental homeostatic and neurophysiological principles that govern sleep timing and architecture. However, knowledge gained from sleep disorder research and its translation to medicine have been somewhat unidirectional. Fewer studies examine how the findings in the field of sleep have been translated to MetS and its components. Numerous epidemiological studies have shown a potent association between sleep complaints and MetS. For example, sleep fragmentation and chronic sleep deprivation were found to influence the development and/or progression of obesity, hyperlipidemia, hypertension, and diabetes (Suliman et al., 2018). Deeper understanding of the physiology of sleep may provide mechanistic and testable explanations for the association between sleep and MetS.

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