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The Effect of Circadian Rhythm on Obesity

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Abstract: Obesity is a state of overaccumulation, leading to a weight higher than normal data. The rate of obesity is increasing quickly; over-eating, a shortage of exercise, and the alteration of daily routines play significant roles in it. It represents one of the most significant challenges in contemporary health discussions. Circadian rhythm disruption influences hormonal levels and alters digestive and eating patterns within the body. However, reaching a comprehensive consensus on how the biological mechanisms of circadian rhythms directly contribute to obesity remains a challenging task. This review will classify circadian rhythms as a key factor in obesity by looking at how they affect conditions like metabolic syndrome that may be related to obesity and how they change the body's physiological states. It further suggests integrating circadian rhythm research into investigations of obesity's etiology to uncover its influence on internal mechanisms. For the application, by monitoring metabolite levels in specific groups, like shift workers and those in high-stress, high-intensity jobs, to preemptively identify individuals who are at higher risk for obesity or not. Consequently, this can prompt the development of personalized prevention and treatment strategies tailored to diet, exercise, and rest regimens for these populations.

Keywords: circadian rhythms, obesity, metabolism

1. Introduction

According to the WHO, obesity is characterized by an unhealthy accumulation of body fat that can negatively impact health [1]. And can be quantified by a high body mass index (BMI). Individuals whose BMI is equal to 25 kg/m² or higher than it will be classified in the obesity group [2]. Since the development of the Industrial Revolution, more and more factories opened around 24 hours with a substantial workforce of shift workers. Concurrently, in regions where food shortage is no longer a concern, people often overeat and stay up late, leading to various rhythm-related health problems. According to the "2023 World Obesity Report," the global obesity rate was 42% in 2020, with projections suggesting it may surpass 54% by 2035 [3]. The fact that genetic factors may play a role in obesity is found in numerous studies, nevertheless, insufficient physical exercise, habitual overeating, and some other lifestyle factors must not be overlooked. Moreover, obesity significantly impacts physiological functions, leading to various diseases, including diabetes and cardiovascular conditions [4]. The following figure illustrates the regional distribution of obesity and associated health issues worldwide [2].

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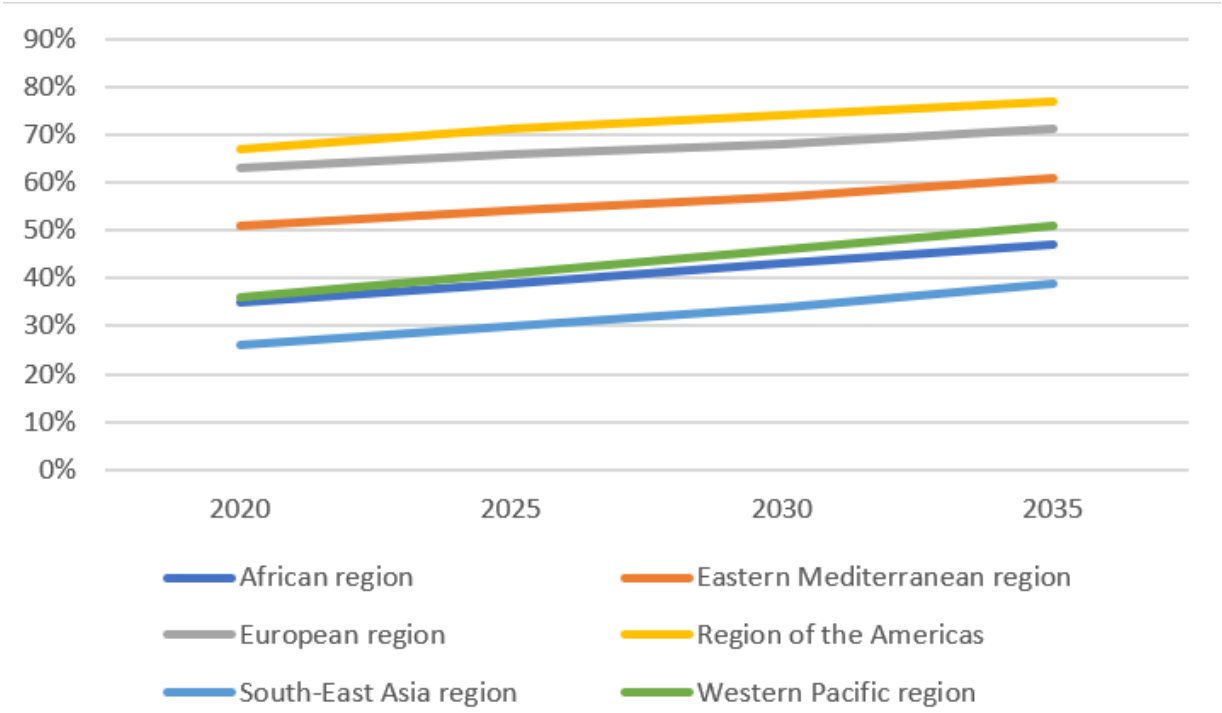

Figure 1: Overweight and obesity (high BMI) rate in different areas

The circadian rhythm has a key influence on physiological processes. For example, a rhythmic pattern leads to eating and digestion cycles in the digestive system [5]. The cellular redox state modulates CLOCK/BMAL1 and NPAS2/BMAL1's transcription, controlled by nicotinamide adenine dinucleotide NAD(H) and NADP(H) cofactors. Some studies showed that the abnormal levels of them lead to metabolic chaos. The evidence indicates that circadian rhythms change due to CLOCK/BMAL1 alteration, breaking the inner physiological balance, and the obesity risk is increased. When the cofactors are in reduced form, the binding efficiency to DNA increases; conversely, when oxidized, the efficiency decreases. NAD, playing a critical role in redox reactions and serving as a substrate for SIRT1, in the livers of ClockΔ19/Δ19 and Bmal1-/- mice exhibits significantly lower levels, highlighting its regulation by circadian rhythm-controlled genes [6]. In addition to the genes that regulate the circadian rhythm influencing metabolic components, metabolic organs also have inherent rhythmicity. For instance, the concentrations of metabolic hormones such as glucocorticoids, insulin, and leptin levels in peak during the period of highest human activity within a 24-hour cycle.

Compared to those regular daily workers in the day, altered circadian rhythms, exemplified by shift workers, exhibit a higher incidence of metabolic syndrome [7]. Research also indicates a strong association between metabolic syndrome (MetS) and obesity [8]. MetS is a group of diseases that raise the risk of heart disease and stroke. These include overweight (especially the middle), high blood pressure, high blood sugar, high triglycerides (TG), and low HDL-c [9]. Finding the association between circadian rhythms and obesity enhances our comprehension of the underlying mechanisms of obesity and supports the creation of time-based biological interventions, enabling early prediction and prevention of obesity through personalized strategies. Moreover, type 2 diabetes and cardiovascular diseases global rates are influenced by obesity, significantly straining healthcare systems. Through a clear understanding of this relationship, doctors can design targeted strategies, such as establishing stable night shift schedules, promoting healthier eating habits, or limiting the frequency of shift work per week, used to address obesity at its root. This review focuses on Circadian

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Control of Energy. Metabolism and obesity risks, indicating that circadian rhythm disruption plays an important role in obesity.

2. Circadian control of energy metabolism

2.1. Hormonal regulation

MetS frequently serves as the main reason for obesity. To make the link clear, some studies posted the connection between circadian rhythms and insulin secretion, as well as the impact on glucose homeostasis. Research has demonstrated that glucose tolerance fluctuates during the day, mostly reaching its highest levels in the morning and declining at other times. Additionally, some studies have noted that the glucose tolerance of healthy individuals in the morning is similar to that of diabetic patients at night [10]. This finding suggests that glucose metabolism is more efficient, and insulin secretion is higher in the earlier part of the day. Therefore, we can deduce that the circadian rhythm of human activity closely aligns with insulin and glucose homeostasis. Leptin, as a type I cytokine, is synthesized in adipose tissue and secreted into the bloodstream, maintaining energy homeostasis by modulating both energy intake and expenditure to achieve metabolic stability. Research has demonstrated that the leptin gene mutations can disrupt normal metabolic processes, always leading to hyperphagia and obesity among affected individuals. Ghrelin, a protein produced by cells lining the stomach, has similarities to certain gut microbiota, stimulating appetite through its orexigenic effects within the gastrointestinal system. Despite the absence of ghrelin having no giant influence on food consumption or body weight among wild-type individuals, medications derived from ghrelin have been shown to influence eating behavior [11]. The evidence suggests that ghrelin has an influence on regulating appetite, but it is not the primary factor in controlling food intake. In the context of MetS, there is an increased peripheral metabolic activity of cortisol within the body, contributing to greater abdominal fat deposition in females [12].

2.2. Chrono nutrition and metabolic timing

The circadian rhythm, a crucial component of the human body's regulatory systems, influences various physiological processes, including eating and digestion patterns. Having meals at three fixed times is a daily routine of humans nowadays, similar to the period of heightened activity. Over evolutionary time, digestive rhythms have synchronized with these meal schedules. However, modern social schedules such as shift work and other circadian rhythm disruptions lead to irregular eating habits, particularly evening eating. In a study, participants are categorized based on different kinds of eating time, then utilized questionnaires to assess participants' subjective experiences, and analyzed blood samples to compare metabolite levels. The researchers found that the secretion of hormones that regulate appetite is changed in the late eating group, leading to increased hunger and decreased energy expenditure during waking hours. Consequently, late eating leads to weight gain by increasing food intake and reducing overall energy consumption [13]. In summary, evening meals may affect metabolic processes and contribute to obesity. Recently, various treatment strategies for obesity have proliferated, and time-restricted feeding (TRF) is one of the most promising approaches. By restricting the daily eating window, TRF helps synchronize hunger cues and digestive processes, which then minimizes the risk of excessive fat accumulation. In the initial application, TRF was implemented in obese mice, demonstrating that it prevented weight gain without altering food intake or physical activity levels. Moreover, TRF can enhance nutrient utilization efficiency (improving digestion and absorption), and from an environmental perspective, it can also be seen as a sustainable practice [14].

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3. Circadian disruptions and obesity risk

3.1. Shift work and metabolic dysfunction

A study examined the prevalence of obesity among female nurses who were engaged in shift work. The results indicated that in the time-type matching cohort (n=317), 88 participants were identified as obese. In contrast, the time-type mismatch group (n=167) also exhibited a significant obesity rate, with 55 cases identified [15]. As a result, shift work is an important factor that leads to obesity. Additionally, a further analysis compared shift workers to day and night workers, revealing that shift workers had an average weight gain of 2-3 kilograms compared to the other two groups. Their BMI was elevated by approximately 0.1-0.8 points, and their waist circumference was increased by roughly 1.5-2.1 cm. These findings collectively highlight the substantial influence of shift work on obesity [16].

The mechanism of the shift work influence on obesity has been explored by previous researchers, who initially focused on its effects on metabolite levels. By comparing blood metabolite levels between shift-working nurses and those on regular schedules, 21 types of glycerophospholipids and sphingolipids reducing were observed, while aspartic acid, serotonin, and taurine levels were elevated [17]. This suggests that shift work induces changes in certain metabolite levels, potentially triggering early biological alterations associated with obesity. In terms of energy balance, the fatigue induced by shift work often results in workers opting for high-calorie foods over nutritionally balanced meals. This not only increases calorie intake but may also lead to deficiencies in trace elements. Regarding energy expenditure, shift workers, including nurses, typically experience lower work intensity during night shifts, leading to a decrease in basal metabolic rate (BMR). Consequently, excess calories are more likely to be stored as fat in the body [18]. That is a bad circulation so that the shift workers will be fatter and fatter day by day. These findings stress how shift work can disrupt both energy intake and expenditure, contributing to obesity.

3.2. Sleep deprivation and weight gain

An analysis of how shift work influences weight maintenance reveals that, among shift workers, approximately 50% of participants have an increase in weight ranging from 9.1 to 11.3 kilograms since they began their irregular work schedules. Furthermore, these individuals only averaged 6.38 hours of sleep per night. Regarding eating habits, many reported thinking of food even outside of regular meal times. Even the mere scent of food or an accidental glimpse could provoke a desire to eat. This brings about insufficient sleep, common among shift workers, which is associated with a notable rise in appetite [19]. Sleep deprivation can disrupt the normal secretion of hunger-related hormones. For example, ghrelin levels tend to rise continuously in individuals who experience multiple consecutive days of inadequate sleep. In the case of leptin, its concentration typically fluctuates throughout the day—decreasing during daytime hours, which increases appetite, and rising at night. However, sleep-deprived people often see a reduction in leptin levels even during nighttime, leading to heightened appetite [20]. The factors contributing to weight gain frequently originate from inadequate and single types of food intake, leading to insufficient absorption of consumed calories, such as reduced fiber consumption. According to prior research, individuals with short sleep durations and irregular sleep patterns, like shift workers, tend to experience a substantial increase in appetite beyond normal levels. Despite this increased appetite, they are unable to efficiently utilize the consumed calories, which results in excess fat accumulation, ironically [21].

Scientists discovered the connection by considering circadian rhythm disturbances in obesity studies. This factor not only influences the release of hormones within the body but also alters personal appetite and the inclination to consume food during unconventional eating hours. Currently,

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the majority of studies examining the effects of circadian rhythm disruptions on physiological factors, such as hormone levels and appetite, rely on methodologies like cross-sectional analyses. These involve briefly exposing participants to altered day-night cycles or having them retrospectively complete questionnaires. Such approaches tend to introduce a higher degree of uncertainty in their findings. Therefore, it would be more beneficial to adopt longitudinal study designs when choosing research methods. Moreover, there is a link between hormone levels and obesity, as previously noted. Researchers can identify individuals at elevated risk for obesity and subsequently create tailored prevention strategies focused on diet, sleep, and physical activity by monitoring irregularities in hormone levels through blood tests.

4. Conclusion

To summarize, circadian rhythm disruption influences obesity significantly through a variety of mechanisms. Hormones and metabolic processes levels regulation, the sense of appetite, the function of digestion, use, and storage of nutrients are influenced by it, creating an interconnected cycle. For example, the behaviors of shift work and sleep deprivation break the balance of the circadian clock and metabolism, leading to the high risk of Mets and obesity. Moreover, numerous studies have established that circadian rhythm disruption changes eating habits, increasing the sense of hunger and decreasing the consumption of energy at night, and over accumulation brings obesity. Historically, obesity research has mostly focused on daily dietary patterns, food types, and the frequency and intensity of physical exercise, often neglecting the crucial function of circadian regulation. Researchers should integrate circadian biology as a core element in their studies of obesity. Using a longitudinal study to reduce the uncertain factors during the investigations so that the high obesity risk individuals can be found through metabolite and hormone level detection, then scientists design some targeted prevention and treatment plans; the obesity problem can be solved from its roots.

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