

Progress in Circadian Rhythm Effects on Human Metabolism and Emotion

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Abstract. The circadian rhythm is an endogenous timing system that precisely regulates physiological processes related to metabolism and emotions through a hierarchical network of the main clock in the hypothalamic suprachiasmatic nucleus (SCN) and peripheral tissue clocks. Disruptions in the rhythm caused by modern lifestyles (such as shift work, night lighting, and irregular eating) are significantly associated with diseases such as obesity, type 2 diabetes and depression. Abnormalities in core clock genes, inflammation activation, insulin resistance and dysregulation of the gut-brain axis constitute a shared pathway for the metabolic-emotional comorbidity. Interventions based on rhythms, such as time-restricted eating (TRE) and the light management, show preliminary evidence-based support in improving weight, blood sugar, mood, and quality of life. In the future, high-quality, large-sample randomized controlled trials are needed to verify the long-term efficacy and safety of these interventions, and to further clarify the optimal time windows, target populations, and combined intervention models for individualized protocols, thereby promoting the translational application of circadian rhythm-based strategies in precision medicine.

Keywords: Circadian Rhythm; Metabolism; Emotion.

1. Introduction

Life is a cyclical process. This cyclical nature is not simply repetitive; rather, it is a dynamic and directional oscillation, with the overall trend being towards aging. However, within the larger life cycle, there are countless smaller cycles that maintain the overall stability and continuity of the system. The circadian rhythm refers to the daily (24-hour) life activity rhythm, driven by an internal clock and influenced by many external factors. Ancient people recognized long ago the importance of having a regular daily routine for maintaining good health. The molecular mechanism of the circadian rhythm underwent groundbreaking innovative discoveries in the 1980s and became one of the 125 important scientific questions proposed by the international top scientific journal Science on its 100th anniversary and gave rise to the Nobel Prize in Physiology or Medicine in 2017 awarded to Jeffrey C. Hall, Michael Rosbash, and Michael W. Young for their research on the biological clock mechanism of individual cells [1].

The physiological impact of circadian rhythms extends far beyond the regulation of sleep. The suprachiasmatic nucleus (SCN) located in the hypothalamus serves as the main clock, coordinating the peripheral clocks throughout the body through neural projections, hormonal signals, and thermoregulatory rhythms, forming a hierarchical timing network. This network precisely regulates metabolic processes, including glucose uptake, insulin secretion, lipid synthesis and breakdown; at the same time, circadian genes also profoundly influence neurotransmitter metabolism, synaptic plasticity, and the functional activities of brain regions related to emotions. However, modern lifestyles, such as the shift work, nocturnal light exposure and the irregular eating, cause the internal rhythm to be disconnected from environmental signals, resulting in a "circadian rhythm disorder" state. Epidemiological data and clinical studies consistently show that rhythm disorders are significantly associated with metabolic diseases such as type 2 diabetes and obesity, as well as mental disorders such as depression [2].

This paper aims to systematically review the molecular and the neural circuit mechanisms of circadian rhythm regulation of metabolism and emotions, clarify how the circadian rhythm disorders drive metabolic and emotional abnormalities, including their comorbidities, and assess the evidence-based basis of intervention strategies based on the circadian principles, providing a reference framework for integrated research in this field.

2. Disrupted Circadian Rhythms on Metabolic Diseases

2.1. Disrupted Circadian Rhythms and the Obesity

Obesity is one of the fastest-growing metabolic diseases worldwide. Its occurrence is not only related to excessive energy intake and insufficient physical activity but also significantly influenced by abnormal biological rhythms. In recent years, research on "chrononutrition" found that there is a close connection between the meal times and body's circadian rhythms. Long delays in dinner time, nocturnal eating, and irregular eating patterns can all lead to an imbalance in energy metabolism, thereby increasing the risk of obesity.

Studies have found that there is an independent circadian rhythm system in human adipose tissue that can regulate the fat production, fat breakdown, and the expression of inflammatory factors. When the circadian rhythm is disrupted, the clock genes in adipose tissue express abnormally, leading to increased fat accumulation. An animal study showed that specifically knocking out the BMAL1 gene in the fat cells would result in inhibition of fat breakdown and cell hypertrophy, confirming its key role in maintaining the balance of energy [3].

Due to the inconsistency between work hours and the natural light-dark cycle, shift workers usually have problems such as the insufficient sleep, nocturnal eating, and changes in hormone rhythms. A retrospective cross-sectional study included 9,322 employees (4,039 long-term night shift workers) from a semiconductor factory in Taiwan. Using data from the 2019 health check-ups, it analyzed the association between night shift work and metabolic syndrome. The results showed that the body mass index (BMI) of night shift workers was 0.3 kg/m² higher than that of day shift workers (25.1 vs 24.8), the waist circumference (WC) was 0.9 cm larger (80.7 vs 79.8 cm), and the rate of overweight/obesity was 3.6% higher (54.3% vs 50.7%), with all differences being statistically significant. Age stratification showed that night shift workers over 30 years old had significantly higher BMI and WC. After adjusting for age, gender, and BMI, night shift work increased the risk of metabolic syndrome by 17% (OR = 1.17) [4].

2.2. Disruption of Circadian Rhythm and Diabetes

The core characteristics of type 2 diabetes are insulin resistance and abnormal glucose regulation. The circadian rhythm plays an important role in pancreatic function and glucose metabolism. Under normal circumstances, the insulin secretion capacity of pancreatic β cells shows significant diurnal variations. During the day, with increased human activity, the demand for glucose rises, resulting in higher insulin sensitivity; at night, when the body enters a rest state, glucose tolerance decreases. If high-calorie foods are consumed at night for a long time, it is likely to cause post-meal blood sugar elevation and increased insulin burden.

A prospective cohort study included 84,790 middle-aged and elderly participants from the UK Biobank (average age 62.3 years, 58% female), who wore wrist-mounted light sensors to continuously record approximately 13 million hours of individual light data for one week, and tracked new cases of type 2 diabetes over an average of 7.9 years (a total of 1,997 cases). The study used the Cox proportional hazards model, adjusting for demographic, socioeconomic, lifestyle, multi-gene risk score, and amplitude and phase estimated by the circadian rhythm model to control for confounding factors. The results showed that the brighter the nighttime light (00:30 - 06:00), the risk of diabetes increased in a dose-dependent manner: compared with the darkest group (0 - 50 percentile), the risk ratios for the 50 - 70, 70 - 90, and 90 - 100 percentile groups were 1.29, 1.39, and 1.53 (all $P < 0.0001$),

respectively; brighter daytime light was associated with a reduced risk (but not significant after adjusting for lifestyle). The estimated reduction in circadian rhythm amplitude and phase shift also independently predicted a higher risk, and nighttime light and genetic risk independently overlapped [5].

In addition, abnormal core clock genes are also associated with the occurrence of diabetes. Studies have shown that CLOCK and BMAL1 not only regulate pancreatic β cell function but also affect the process of hepatic gluconeogenesis. When the biological clock is disrupted, liver glucose output increases, insulin sensitivity decreases, thereby promoting the development of diabetes [6,7].

2.3. Disruption of Circadian Rhythm and Abnormal Lipid Metabolism

Lipid metabolism exhibits a distinct circadian rhythm. The liver, as the primary metabolic organ in the body, regulates the cholesterol synthesis, fatty acid oxidation, and triglyceride storage through its circadian rhythm.

A study confirmed that both the endogenous cholesterol synthesis and the bile acid synthesis in the human body are regulated by circadian rhythm: cholesterol synthesis markers (such as the mevalonate, lanosterol) peak at night, consistent with the activity of HMG-CoA reductase; while the bile acid synthesis marker C4 peaks during the day, showing an inverse fluctuation, which indicates the sequential coordination and separation characteristics of key metabolic pathways [8].

Another systematic review included 9 observational studies (5 cross-sectional and 4 cohort studies) to comprehensively assess the association between shift work and metabolic-related fatty liver disease (MASLD). Most studies showed that shift work increases the risk of MASLD, and there is a dose-response relationship, especially for those with long-term or frequent shift work, the effect is stronger. Subgroup analysis suggested that gender, age, lifestyle, sleep timing, and occupational factors may modify this association, and BMI was confirmed as a partial mediating factor [9].

In addition, insufficient sleep can alter the expression of inflammatory-related genes in adipose tissue and increase the levels of pro-inflammatory factors. Chronic inflammatory state further promotes insulin resistance and atherosclerosis formation. Therefore, circadian rhythm disorders may increase the risk of cardiovascular diseases by affecting lipid metabolism and inflammatory responses.

3. Circadian Rhythm Disruption and Emotion

The influence of circadian rhythm disruption on emotion manifests at multiple levels. A cross-sectional study from the UK Biobank found that for every five-point decrease in the relative amplitude of circadian rhythm ($n=91,105$), the lifetime risk of major depressive disorder increased by 6%, bipolar disorder increased by 11%, the happiness score decreased by 9%, and this risk remained significant after adjusting for confounding factors [10].

In clinical studies, circadian rhythm phenotypes (chronotype) have a specific association with dimensions of mental symptoms. A study published by Balter et al. in *Translational Psychiatry* ($N=515$) found that 11 out of 13 psychiatric traits (including depression, obsessive-compulsive disorder, social anxiety, and delusional ideation) were associated with the evening-type (evening-oriented) tendency, while only the manic trait was associated with the morning-type. This study further discovered through daily multiple ecological instantaneous assessments that evening-type individuals exhibited significantly lower drive and motivation from morning to evening, and more obvious negative emotions and ADHD-type symptoms in the evening [11].

The neural mechanism by which circadian rhythm affects the emotion involves multiple levels, such as core clock genes (such as *Bmal1*, *Clock*) that drive approximately 50% of mammalian gene rhythmic expression through a transcription-translational feedback loop and their polymorphisms are associated with emotional disorders such as depression. The master clock SCN regulates local clocks in emotion-related brain regions (such as the prefrontal cortex, nucleus accumbens, and amygdala) through neural projections. At the cellular level, clock genes regulate neuronal excitability, synaptic

plasticity, and neurotransmitter release - these core physiological functions ultimately affect emotional behaviors through cell type-specific mechanisms. Additionally, stress can disrupt the rhythm, and rhythm disruption itself can also induce emotional disorders, forming a bidirectional vicious cycle [12].

4. Disrupted Rhythms as a Shared Pathway for the Metabolic-Emotional Co-morbidity

4.1. Inflammation: The Bridge between Metabolism and Emotion

Disrupted rhythms promote the low-grade chronic inflammation: On one hand, it triggers endotoxin entry into the bloodstream through damaged intestinal barriers and dysbiosis; on the other hand, it releases pro-inflammatory factors through hypoxia in adipose tissue and infiltration of macrophages. These inflammatory mediators can cross the blood-brain barrier or affect the central nervous system through vagus nerve signals, activating microglia and reducing the secretion of brain-derived neurotrophic factor (BDNF) in the hippocampus, thereby impairing emotion regulation. Inflammation may be the most important mediator driving the co-morbidity of metabolism and emotion in rhythm disorders [2].

4.2. Insulin Resistance and Brain Energy Metabolism

Insulin resistance is not only the core pathology of type 2 diabetes but may also directly affect brain function. Neuronal insulin signaling is involved in synaptic plasticity, dopamine transporter function, and food reward processing. Systemic insulin resistance caused by rhythm disorders may indirectly affect the brain insulin signaling through impaired brain insulin signaling [2].

4.3. Rhythmic Regulation of the Microbiota-Intestine-Cerebral Axis

The composition and function of the intestinal microbiota fluctuate in a circadian rhythm and are strongly shaped by feeding rhythms. Disrupted rhythms alter the microbiota rhythm, affecting the circadian release of short-chain fatty acids, bile acids, and other metabolic products, which through the gut-cerebral axis influence the inflammatory state and neurotransmitter metabolism of the central nervous system [13].

5. Interventions Based on Circadian Rhythm Regulation

5.1. Time-restricted eating (TRE)

In recent years, time-restricted feeding has become an important method for regulating the circadian rhythm. This approach emphasizes completing meals within a fixed time window each day and avoiding excessive calorie intake at night.

A randomized controlled trial (RCT) involving 61 obese patients (average BMI 35.5 kg/m²) was conducted, randomly divided into the time-restricted eating (TRE) group (with daily self-selected 10-hour eating window) and the standard treatment (SOC) group (only receiving Mediterranean diet counseling), with an intervention period of 12 weeks. The results showed that the TRE group lost 4.6 kg (-4.6%) in weight, significantly better than the 1.7 kg (-1.7%, $p < 0.001$) lost by the SOC group, and the weight loss mainly came from fat reduction and visceral fat reduction, indicating that TRE is a safe and effective weight loss intervention measure [14].

A randomized controlled trial (RCT) for patients with metabolic syndrome (162 cases) showed that 3-month time-restricted eating (TRE, 8-hour eating window) significantly improved multiple aspects of quality of life (such as physical function +5.2, social function +9.1, role-emotion +22.4, all $P < 0.01$), sleep efficiency (+0.29, $P = 0.021$), and stress levels (-2.2, $P = 0.003$), and reduced GLP-1 (-0.9 pg/mL) and increased pancreatic polypeptide (+8.9 pg/mL) [15].

Another RCT published in 2026 aimed to explore the efficacy of TRE combined or not combined with calorie restriction, compared with traditional calorie restriction, in obese patients with severe depression. The study planned to recruit 90 patients, randomly divided into three groups: the simple TRE group (8-hour eating window), the TRE combined with calorie restriction group (75% of calories), and the simple calorie restriction group, with an intervention period of 24 weeks. The main outcome was the change in depression score, and secondary outcomes included weight, waist circumference, body composition, metabolic indicators (blood sugar, insulin, lipids, etc.), circadian rhythm, and quality of life. The study hypothesized that TRE might be superior to simple calorie restriction by improving metabolism, rhythm, and inflammation, but the results have not been published, and this scheme provides a methodological framework for subsequent clinical trials [16].

5.2. Lighting Management

Lighting is the strongest environmental factor in regulating the human biological clock. A randomized controlled trial published in "Frontiers in Psychiatry" included 48 depressed inpatients and randomly divided them into a bright light group (receiving 30-minute, 10,000 lux full-spectrum white light exposure (color temperature 6000K, wavelengths > 450nm blue light unfiltered, n=24) and a control group (receiving 100 lux dim light, n=24), for a duration of 2 weeks. The results showed that the fasting blood glucose in the bright light group significantly decreased (95% CI: 0.280-0.600, $p<0.001$), the median value of cortisol decreased (95% CI: -2.677 to -0.064, $p=0.040$), and the amplitude decreased ($p<0.05$); the blood glucose changes in the bright light group were positively correlated with the median value of cortisol changes ($\beta=0.053$, 95% CI: 0.016-0.122, $p=0.036$), and were also positively correlated with the improvement of the depression scale score ($\beta=0.531$, $p=0.042$). Thus, it can be seen that bright light resets the circadian rhythm, reduces cortisol levels, and indirectly improves insulin sensitivity, thereby exerting a hypoglycemic effect [17].

At the same time, the management of the dark period is also important. Reducing blue light exposure before bedtime and maintaining regular sleep-wake times help to consolidate the stability of the melatonin and cortisol rhythms.

A randomized, single-blind, cross-over controlled trial included 39 Japanese male children with myopia aged 10-12 years old, evaluating the effects of wearing 40% blue light-blocking glasses (compared to ordinary corrective lenses) 3 hours before bedtime on saliva melatonin, sleep phase, and daytime behavior, lasting for 5 weeks (including a 2-week intervention period and a 1-week washout period). The results showed that the blue light glasses did not change melatonin secretion, but significantly advanced the bedtime (about 6 minutes) and the time to sleep, and the effect was more obvious in the second week; it also significantly reduced irritability, aggressive behavior, and morning bad mood [18].

An ongoing randomized controlled trial specifically targets individuals with prediabetes or type 2 diabetes and who have "social jet lag" (i.e., irregular schedules on weekdays and weekends). The intervention plan combines morning bright light therapy and wearing blue light-blocking glasses in the evening, aiming to improve glucose metabolism by adjusting sleep-wake times. This provides a direct clinical trial design basis for the value of "maintaining regular sleep" intervention [19].

6. Conclusion

This article systematically reviews the core role of circadian rhythms in metabolic and emotional regulation and the multi-level mechanisms by which their disruption leads to diseases. Current evidence indicates that circadian rhythm disorders, through pathways such as molecular clock dysregulation, central-peripheral clock disassociation, chronic inflammation, insulin resistance, and rhythmic changes in the gut microbiota, jointly drive the occurrence and development of obesity, diabetes, and emotional disorders, and constitute a shared pathological basis for comorbidities. Interventions based on circadian rhythms, such as timed feeding and light management, have shown potential in short-term clinical trials to improve metabolic indicators (such as body weight and blood

sugar) and psychological symptoms (such as depression scores), but their long-term effects, optimal intervention windows, and individualized schemes still need to be verified. Current research is heterogeneous, and some mechanisms are still based on animal or cross-sectional evidence. In the future, it is necessary to combine multi-omics and time-series analysis to conduct large-sample, long-term randomized controlled trials and explore combined intervention models under precise phenotypic classification, in order to transform circadian rhythm regulation into evidence-based practices for the prevention and treatment of metabolic and mental disorders.

References

- [1] Huang Rongfeng, Zhou Runchao, Cao Yuxin, et al. Circadian Rhythm and Obesity: Does There Exist the Best Time for Living? [J]. *Nature Magazine*, 2026, 48(3): 217-227.
- [2] Lloyd M, Prakash BA, Zhao L, Ni G, Ru Y, Vasudevan SR. Circadian rhythms in metabolism and mental health: a reciprocal regulatory network with implications for metabolic and neuropsychiatric disorders. *Curr Opin Physiol*. 2025 Sep;45:None.
- [3] Ishii H, Kitaura S, Wada T, Shimba S. Deletion of Arntl, a component of the molecular clock, in adipocytes leads to cellular hypertrophy by increasing insulin sensitivity via FGF21. *NPJ Biol Timing Sleep*. 2025 Feb 3;2(1):6.
- [4] Lin SC, Yeh WC, Liu ZX, Hsu HF, Chen JY. Night-shift work and its association with metabolic syndrome. *Medicine (Baltimore)*. 2025 Aug 1;104(31):e43598.
- [5] Windred DP, Burns AC, Rutter MK, Ching Yeung CH, Lane JM, Xiao Q, Saxena R, Cain SW, Phillips AJK. Personal light exposure patterns and incidence of type 2 diabetes: analysis of 13 million hours of light sensor data and 670,000 person-years of prospective observation. *Lancet Reg Health Eur*. 2024 Jun 5;42:100943.
- [6] Yoshino J, Imai S. A clock ticks in pancreatic beta cells. *Cell Metab*. 2010 Aug 4;12(2):107-8.
- [7] Shi D, Chen J, Wang J, Yao J, Huang Y, Zhang G, Bao Z. Circadian Clock Genes in the Metabolism of Non-alcoholic Fatty Liver Disease. *Front Physiol*. 2019 May 8;10:423.
- [8] Schroor MM, Sennels HP, Fahrenkrug J, Jørgensen HL, Plat J, Mensink RP. Diurnal Variation of Markers for Cholesterol Synthesis, Cholesterol Absorption, and Bile Acid Synthesis: A Systematic Review and the Bispebjerg Study of Diurnal Variations. *Nutrients*. 2019 Jun 26;11(7):1439.
- [9] Schroor MM, Sennels HP, Fahrenkrug J, Jørgensen HL, Plat J, Mensink RP. Diurnal Variation of Markers for Cholesterol Synthesis, Cholesterol Absorption, and Bile Acid Synthesis: A Systematic Review and the Bispebjerg Study of Diurnal Variations. *Nutrients*. 2019 Jun 26;11(7):1439.
- [10] Lyall LM, Wyse CA, Graham N, Ferguson A, Lyall DM, Cullen B, Celis Morales CA, Biello SM, Mackay D, Ward J, Strawbridge RJ, Gill JMR, Bailey MES, Pell JP, Smith DJ. Association of disrupted circadian rhythmicity with mood disorders, subjective wellbeing, and cognitive function: a cross-sectional study of 91 105 participants from the UK Biobank. *Lancet Psychiatry*. 2018 Jun;5(6):507-514.
- [11] Balter LJT, Holding BC, Petrovic P, Axelsson J. The rhythm of mental health: the relationship of chronotype with psychiatric trait dimensions and diurnal variation in psychiatric symptoms. *Transl Psychiatry*. 2024 Jun 4;14(1):237.
- [12] Francis TC, Porcu A. Emotionally clocked out: cell-type specific regulation of mood and anxiety by the circadian clock system in the brain. *Front Mol Neurosci*. 2023 Jun 27;16:1188184.
- [13] Crespo MT, Trebucq LL, Senna CA, Hokama G, Paladino N, Agostino PV, Chiesa JJ. Circadian disruption of feeding-fasting rhythm and its consequences for metabolic, immune, cancer, and cognitive processes. *Biomed J*. 2025 Jun;48(3):100827.
- [14] Padilla, E, Manoogian, E, Nguyen, J. et al. TIME-RESTRICTED EATING PROMOTES WEIGHT LOSS AND REDUCTION IN BODY FAT VS STANDARD OF CARE: A RANDOMIZED CONTROL TRIAL IN INDIVIDUALS WITH OBESITY. *JACC*. 2024 Apr, 83 (13_Supplement) 1703.
- [15] Zheng Y, Wang X, Wang J, Yang J, Wang T, Li Q, Zhu W, Wang Y, Sui J, Qiang W, Guo H, Wang Y, Shi B, He M. Effects of time-restricted eating and low-carbohydrate diet on psychosocial health and appetite in individuals with metabolic syndrome: A secondary analysis of a randomized controlled trial. *Clin Nutr*. 2024 Oct;43(10):2316-2324.
- [16] Bagherzadeh-Karimi A, Mesri Alamdari N, Hosseini L, Maghsoumi-Norouzabad L. Investigating the effect of intermittent fasting (time-restricted eating) with and without calorie restriction compared to calorie restriction on anthropometric parameters, depression score, and metabolic factors in patients with major depression disorder and obesity: a study protocol for a randomized controlled trial. *Trials*. 2026 Jun 27;27(1):460.
- [17] Fang J, Li X, Zhu S, Hu Q, Wang T, Yu J, Qin X, Zhu D. The effect of bright light therapy on glycemic control and cortisol rhythmicity in depression: a randomized controlled trial. *Front Psychiatry*. 2026 Feb 11;17:1743465.

- [18] Maeda-Nishino NJ, Yoshimoto R, Ono T, Chiba S, Nishino S. Partial blue light blocking glasses at night advanced sleep phase and reduced daytime irritability, disruptive behavior and improved morning mood, but did not alter salivary melatonin secretion in Japanese male schoolchildren. *PLoS One*. 2025 Oct 30;20(10):e0332877.
- [19] Bouman EJ, Slebe R, Stenvers DJ, Elders PJM, Beulens JWJ, Rutters F. A randomized controlled trial to assess if changing sleep timing can improve glucose metabolism in people with prediabetes and type 2 diabetes. *Trials*. 2024 Jul 12;25(1):474.