

Feeding and Eating Disorders in the Context of Circadian Rhythms

ABSTRACT

A circadian rhythm is a 24-hour rhythm controlled by a master clock, the suprachiasmatic nucleus, and driven by synchronizing internal/external zeitgebers. Food intake is one of the most important external cues/zeitgebers. Studies in humans and animals have shown that misalignment of food intake leads to chronodisruption, which is associated with metabolic disruption, obesity, and disordered eating attitudes. The term *chronotype*, which expresses the circadian typology, has been classified into 3 main types that represent the differences in the reflection of circadian rhythms shown in human studies on daily behaviors. It has been reported that evening-type individuals are more prone to disrupted eating attitudes, such as skipping meals, eating at night, and consuming a calorie-rich diet. In addition, eating disorders up to the diagnostic level is associated with the evening type. The bidirectional relationship between impaired circadian rhythms and disordered eating attitudes has brought chronotherapeutic interventions, which are biological rhythm-oriented treatment approaches, to the agenda. Bright light therapy has been found to reduce bulimic eating behaviors and night eating symptoms. More evidence is needed regarding the effect of chronotherapeutic approaches on metabolic disorders, disordered eating attitudes, and eating disorders associated with obesity.

Keywords: Binge-eating disorder, circadian rhythm, night eating syndrome, suprachiasmatic nucleus

Introduction

The concept of biological rhythm refers to cyclic changes corresponding to the time-dependent organization of the environment. Biorhythms are divided into different groups according to their duration. For example, those shorter than 24 hours are ultradian, whereas those longer than 24 hours are called infradian rhythm. Circadian rhythms are approximately 24-hour endogenous rhythms and are reflected in physiological and behavioral changes. It has been observed in many lifeforms, from bacteria to humans, that circadian rhythms affect biological variables, such as the body temperature, heart rate, and blood pressure; various hormone levels, such as melatonin and cortisol; and the sleep-wake cycle. All these variables show periodicity in the 24-hour interval.¹

Although there are many timers (oscillators) that regulate the circadian rhythm, the main center is the suprachiasmatic nucleus (SCN), which is located in the hypothalamus and controls many physiological variables, such as the sleep-wake cycle, body core temperature rhythm, and release of some hormones (melatonin, growth hormone, and cortisol).² It is defined as the "master clock," and it is the main center that synchronizes our circadian rhythm to the rhythm of the outside world. In addition to the SCN, there are many secondary rhythm regulators (peripheral oscillators), such as the peripheral organs (liver, intestine, etc.). Peripheral oscillators include behavioral characteristics, such as eating behavior. The SCN regulates the biological rhythm with the light-dark information coming from the outside and the information received from peripheral oscillators.^{3,4}

The term *chronotype* expresses the inter-individual variation in circadian rhythm.⁵ In addition to genetic and biological factors, sociodemographic characteristics and psychosocial



Ali Kandeğer¹ 

Ümran Eğilmez¹ 

Yavuz Selvi^{1,2} 

¹Department of Psychiatry, Selçuk University School of Medicine, Konya, Turkey
²Neuroscience Research Center, Selçuk University School of Medicine, Konya, Turkey

Corresponding author:
Ali Kandeğer ✉ dralikandeger@gmail.com

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and geographic factors play a role in the formation of this circadian typology.⁶ Chronotype studies and the scales used in chronotype determination basically divide the chronotype differences into 3 types—morning, intermediate, and evening.⁷

For individuals with the morning chronotype, the rise and fall in daily physiological variables occur earlier in the day than they do in the intermediate and evening chronotypes (phase advance). These individuals feel better in the morning regarding physical and mental performance and prefer to be active early in the day. Morning chronotype characteristics are more common in women than men and in older individuals compared with young people. The change of these values in the evening-type individuals occurs later in the day compared with the morning and intermediate types (phase delay). Evening-type individuals experience better performance in the afternoon and evening; therefore, they are preferably active late in the day. Approximately 40% of adults have one of the 2 extreme chronotypes; the rest are in the middle of the spectrum.^{8,9}

Although chronotypes express the differences between individuals in the synthesis of biological, physiological, behavioral, and social rhythms, studies are showing that having the evening type is more associated with some psychiatric symptoms and disorders. It has been reported that the prevalence of mood disorders, substance use, and sleep disorders increase in evening chronotypes.¹⁰⁻¹² Studies and systematic reviews emphasize that evening-type individuals are more prone to symptoms, such as difficulty in emotion regulation, negative eating behaviors, impulsivity, smoking, and substance use, as well as psychiatric disorders, such as mood disorders, anxiety disorders, and addiction.^{13,14}

In this review article, feeding behavior and eating disorders will be examined in the context of circadian rhythms. In addition, the role of circadian rhythm-oriented interventions in treatment is discussed.

Circadian Control of Food Intake

As with other physiological variables in humans, energy/food intake can be predicted within the framework of the circadian system. Food intake in humans occurs during the active phase, and thus, energy stores are renewed. In contrast, the emptying of the energy stores and the fasting time corresponds to the inactive phase, including the sleep phase. The eating pattern in humans follows an endogenous rhythm; before the hunger that will last all night and induced by sleep, appetite is increased, and eating is encouraged; in contrast, the satiation value of the foods eaten decreases in the active phase. Thus, it has been suggested that there is a circadian rhythm in the feeding-fasting cycle in humans. It is claimed that food intake is regulated by both homeostatic and circadian mechanisms, reminiscent of the 2 process models of sleep.¹⁵

MAIN POINTS

- *The time of food intake is a robust external stimuli that synchronize the circadian rhythm, and feeding mistiming is associated with chronodisruption.*
- *Evening-type individuals are more prone to chronodisruption, disordered eating attitudes, and eating disorders.*
- *Chronotherapeutic interventions such as bright light therapy may be an effective treatment choice in eating disorders symptoms through improving circadian misalignment.*

The homeostatic process of food intake is based on the balance between orexinergic and anorexic factors. The orexinergic pathways are mainly activated at the beginning of the active phase and gradually increase, shifting the homeostatic process toward “feeding”.¹⁶ In response to the meals consumed, anorexinergic pathways increase satiety during the active phase and ensure that feeding behavior is kept at a minimum level at the beginning of sleep. In the fasting state, ghrelin is released and induces the release of neuropeptide Y (NPY) and agouti-related peptide (AgRP) by providing orexinergic signal transmission to the arcuate nucleus, an energy-sensitive nucleus of the hypothalamus. NPY and AgRP activate secondary messenger neurons in the lateral and perifornical hypothalamic regions.^{17,18} At this time, these activated neurons inhibit oxytocin-expressing neurons and support the stimulation of feeding behavior. After food intake, many hormonal changes occur in the postprandial phase in favor of satiety. The signals of anorexinergic hormones, such as pancreatic insulin, adipocyte-derived leptin, and intestinal glucagon-like peptides, reach the arcuate nucleus, where they stimulate pro-opiomelanocortin (POMC) neurons.¹⁹⁻²¹ The homeostatic process of food intake includes the hyperphagic and hypophagic effects of endocannabinoids that have GABAergic and glutamatergic effects, as well as additional neurochemical processes.²²

The close relationship between circadian control of food intake and clock genes has been shown in animal studies. It has been illustrated that there is a decrease in day–night variation in the food intake pattern of mice with a global deletion in the clock gene, and there is a change in the daily fasting-feeding cycles in general.²³⁻²⁵ It has been suggested that SCN lesions cause behavioral arrhythmia, disrupting the feeding-fasting cycle without any change in the number of meals or the amount of food consumed in the 24-hour cycle. These studies show that SCN has a major role in the daily pattern of feeding behavior.^{26,27} In a study conducted under conditions where the time clue was removed and the participants were alone, feeding rhythms were examined; it was observed that the participants ate 2 or 3 meals spontaneously during their active phase under these conditions. It has been found that this is independent of the circadian rhythm (chronotype) and wakefulness period, which vary considerably between individuals. Based on this, researchers have suggested that eating behavior is strongly influenced by the circadian clock, independent of external stimuli.²⁸

The circadian control of the feeding-fasting cycle—and hence, eating behavior—is mainly based on the interaction between the SCN, which is calibrated with light information from the environment, and food-entrainable clocks (peripheral oscillators). These clocks, which synchronize depending on the food intake rhythm, are located in the brain and adjust the food clock. They also determine the rhythm according to the anticipation of food availability. This system is affected by the time of meals consumed and phase control of the SCN.¹⁵

In a study investigating how mealtimes affect circadian system biomarkers and metabolic parameters through peripheral oscillators, 10 young male participants were taken into a laboratory for 13 days, and the mealtimes were delayed for 5 hours; the effects of these conditions on metabolic parameters, the circadian rhythms of peripheral tissues, and the melatonin and cortisol levels, which are markers of SCN, were investigated. As a result of the research, it was observed that the delay in mealtime did not affect melatonin,

cortisol levels, plasma triglyceride, and insulin rhythms, or clock gene expression rhythms; however, it did cause changes in plasma glucose levels. Based on this, it has been suggested that the rhythm of eating behavior may have a role in, synchronizing circadian rhythms of peripheral tissues and may be the center of attention in patients with circadian rhythm disorders and night eating disorders as shift workers.²⁹

The incompatibility between the rhythms of eating behavior caused by SCN and mealtimes affected by social life, business activities, or personal preferences is also reflected in the rhythms of peripheral tissues. Therefore, eating at the wrong time may cause a disruptive effect. The next section will examine the relationship between this desynchronization and food intake.

Chronodisruption and Food Intake Time

Changes in behavior patterns in different areas (eating, sleeping, working, etc.) may create a mismatch between the environment's endogenous rhythm and time cues. This incompatibility manifests with changes in the oscillators of the circadian system in peripheral tissues and organs.³⁰ These changes include decreased rhythm amplitude, loss of synchronization, and phase mismatch between SCN and peripheral clocks. Eating at the wrong time, exposure to light at night, or working in the resting phase—as in shiftwork—creates desynchronization in the system, and therefore, chronodisruption occurs. Given the circadian regulation of metabolic processes, it is clear that the circadian disruption created by behavioral and environmental factors will also lead to metabolic effects.¹⁵

Studies in humans suggest that circadian disruption in shift workers correlates with the development of obesity and type 2 diabetes mellitus. Moreover, in the short term, the circadian disruption induced by desynchronization has been shown to have adverse effects on glucose tolerance and insulin resistance.³¹⁻³³

There are many metabolic consequences of eating at the wrong time, depending on the diet and species. Studies on rodents have shown higher caloric intake and increased body mass index (BMI) in mice fed in the resting phase than those fed in the active phase.³⁴ In another study, although mice fed in the resting phase had less food intake, it was seen that they gained more weight than those fed in the active phase, and the researchers emphasized the efficiency of the diet as an important parameter.³⁵ When a high-fat diet was given to mice at 2 different times, it was observed that mice fed in the resting phase gained more weight than those fed in the active phase. Based on this, the researchers suggested that the metabolic consequences of a high-fat diet can be alleviated by feeding at the right time.³⁶ Equivalent to skipping breakfast meals, mice that were forced to feed early at night were found to increase weight gain and de novo lipid synthesis.³⁷

In humans, skipping breakfast is associated with increased metabolic risk factors, including obesity and poor glycemic control.³⁸ In addition, it was found that repeated eating in the evening or late at night correlated with an increase in BMI and body fat rate. These findings have not been confirmed in another study in healthy men or women.³⁹ In their study with 209 participants, Muñoz et al⁴⁰ found that those who were given a diet arranged according to chronotype lost significantly more weight than those who received a standard hypocaloric diet.

The daily timing of food intake is important for energy balance in the short and long term. Both chronodisruption and mistimed eating cause an increase in metabolic risk factors. It is clear that the chronotype affecting the daily life habits of the individual will be reflected in eating behaviors and attitudes.

Chronotypes and Disordered Eating Attitudes

Disordered eating describes the full spectrum of eating-related problems from simple dieting to a certain eating disorder. Several studies in the literature have investigated the complex interaction between chronotype and disordered eating attitudes. Interest in this field has been increasing in recent years. It has been reported that morning chronotypes have healthier and more regular eating patterns than the evening chronotypes, and their control of overeating is higher.⁴¹ In a population-based study in which Maukonen et al⁴² included 1,854 people, the researchers reported that having an evening chronotype was associated with later food intake, lower morning energy, and macronutrient intake. The same study reported that the evening type consumed more energy in the evening than the morning type, and there was no difference between chronotypes in terms of total energy intake. The same study reported that evening-type individuals have more irregular eating times and exhibit twofold more food intake on weekend days compared with morning-type individuals.⁴² It has been suggested that eating later in the day simply refers to the circadian rhythm of individuals with the evening chronotype. A small-scale study conducted in the United States showed that evening-type individuals had 2-fold more energy and macronutrient intake after 8 PM compared with the intermediate chronotype.⁴¹

In a cohort-type study including obese individuals with sleep deprivation, Lucassen et al⁴³ reported that morning-type individuals ate smaller portions more frequently, whereas the evening chronotype was associated with eating later, feeding less frequently, and consuming larger portions at a time. In their study on healthcare professionals, Mota et al⁴⁴ reported an inverse correlation between chronotype scores and calorie consumption, and being the evening type led to more food intake, which could be associated with obesity in the long term. In their study on students, Nakade et al⁴⁵ reported that individuals with the evening chronotype have such eating behavior as skipping/restricting breakfast. Moreover, in their study of Brazilian students, in line with the literature, Teixeira et al⁴⁶ reported that evening-type individuals skip breakfast more often and suggested that this could be explained in that their biological rhythm had not yet sent the signal to eat early in the day. In 2 recent studies, researchers reported that individuals with the evening chronotype had a high rate of skipping breakfast, consuming more calories and macronutrients such as sucrose, fat, and saturated fatty acids in the evening, and shifting their food intake to later hours of the day. Thus, it has been shown that evening-type individuals had more unhealthy eating habits in both adolescents and adults.^{47,48}

In the literature, there are studies examining the relationship between chronotype characteristics and the timing and content of eating behavior, and different characteristics of this behavior. Schubert and Randler⁴¹ found that the evening chronotype was associated with more problematic eating behavior (higher disinhibition in eating, higher perceived hunger, lower cognitive control of overeating) in a sample of German students.⁴² Another study conducted on 151 high school students reported that having the evening

chronotype was moderately positively correlated with both bulimic behaviors (binge eating and purging).⁴⁹ In their study on 270 women, Natale et al⁵⁰ reported a relationship between altered eating behaviors and being an evening type. In a study on 1,323 university students, Kandeger et al⁵¹ reported that the evening type was associated with food addiction. In another study involving 383 university students, it was reported that night eating symptoms were associated with the evening chronotype.⁵² In their study with 100 patients who applied to the nutrition and diet outpatient clinic, Harb et al⁵³ found that binge eating behavior was positively correlated with the evening chronotype.

In a large-scale, population-based study conducted in Finland, the relationship of chronotype with depression and emotional eating behavior was investigated. It was found that morning alertness and early morning preference showed a negative correlation with depressive symptoms and emotional eating. In the same study, in accordance with the literature, preferring the late hours of the day and having less morning alertness (preferences compatible with the evening type) were found to be associated with an increase in depressive symptoms and emotional eating attitude.⁵⁴

Although there are many studies in the literature regarding the differences in eating patterns between chronotypes mentioned above, studies examining the relationship between specific eating disorders and chronotype are limited.¹³ Whereas it has been shown that the evening chronotype is more common in patients with eating disorders compared where healthy controls;⁴⁸ there have also been studies that could not detect such a relationship.⁵⁵

Chronotypes and Eating Disorders

The relationship of the SCN with the metabolic and hedonic centers that control eating behaviors and feeding leads to the hypothesis that there may be circadian rhythm disturbance in eating disorders.⁵⁶ Thus, it can be thought that the desynchronization associated with the chronotypes of the individuals related to the timing preferences of daily life activities, such as sleeping, waking up, eating, and social activity, may also contribute to eating disorders. However, in the current literature, there is limited evidence for the relationship between chronotypes and eating disorders.¹³

The evening chronotype, which is more common in people with eating disorders than in the healthy population, is associated with certain mood disorders and insomnia in some studies. Recently, it has been associated with dissociative experiences that may represent 1 of the psychopathological bases of problematic eating behaviors.⁵⁷ In a study involving 783 patients with bipolar disorder, it was reported that individuals with the evening chronotype had higher binge eating, night eating, bulimia nervosa, and BMI values compared with other chronotypes.⁵⁸

Riccobono et al⁵⁹ highlighted the high prevalence of night eating syndrome (NES) in the adolescent population in their study. They included 301 adolescents; these authors showed a significant relationship between evening chronotype and depression, and NES. Similar results were obtained in a sample of 1,136 Italian university students by the same researchers. In addition to the previous findings, it was suggested that there is a total functional circadian delay in NES rather than just a delay in food intake. In addition, in the same study, the researchers emphasized a relationship between

NES and seasonality, and a similar relationship was found with binge eating disorder, bulimia nervosa, and seasonality in the literature.⁶⁰ Considering that having a morning chronotype provides desensitization in terms of seasonality, it can be thought that there may be a complex relationship between evening chronotype, seasonality, and eating disorders.

Natale et al⁵⁰ associated the reduction in symptoms of eating disorders with a shift to the morning chronotype in their prospective study with 46 patients. This result opened the door to chronotherapy in eating disorders.⁵⁰

Chronotherapy in Eating Disorders

Chronotherapy aims to reduce symptoms by regulating the circadian rhythm in disorders caused by circadian shift or disruption. Therefore, studies on chronotherapeutic approaches in mood disorders, sleep disorders, attention deficit hyperactivity disorder, and eating disorders are increasing.⁶¹

Such factors as mistimed eating patterns and phase progression/delay in neuroendocrine hormones, which can be seen in night eating disorders, suggest that chronotherapeutic approaches, such as bright light therapy, can reduce night eating symptoms.^{62,63} Sack et al⁶⁴ reported that bright light therapy applied in the morning is promising for night eating disorder, considering that it will provide phase progression in circadian rhythm. Two case reports in which bright light therapy with an intensity of 10,000 lux was applied in the mornings for 14 days suggested that bright light therapy effectively treats night eating disorder.^{65,66} Following an open-label pilot study, McCune and Lundgren⁶⁷ reported that bright light therapy improved night eating symptoms, sleep, and mood, and side effects were not observed.

Studies on bright light therapy have shown improvement in bulimic symptoms and mood symptoms after therapy.⁶⁸ There have been conflicting results regarding the effects of bright light therapy on bulimia nervosa. Although studies have reported that bright light therapy does not affect the frequency of binge eating and purging,⁶⁹ There is evidence that it significantly reduces these behaviors.^{70,71} Braun et al⁷² reported that there was a significant decrease in binge eating, not purging, during the treatment in the bright light therapy group compared with the control group. Still, they did not find a difference in the frequency of the abstraction behavior.

In a study conducted on patients with anorexia nervosa (AN), it was reported that there was "slight improvement" in core eating pathology assessed by weakness, bulimia, body image dissatisfaction, and interoceptive awareness subscales in a 12-week follow-up after bright light therapy.⁷³ Janas-Kozik et al⁷⁴ reported that BMI, which shows the severity of eating disorders in patients with AN, did not differ between the group that received cognitive behavioral therapy and the group in which 6-week bright light therapy and cognitive behavioral therapy were combined. However, they reported that the group that underwent bright light therapy achieved the targeted BMI increase earlier than the control group did (3 weeks versus 6 weeks). In addition, in both studies mentioned, a significant reduction in depressive symptoms was reported after bright light therapy.

Recently, intermittent fasting, which including interventions that altered eating periods and extended fasting, has been reported

to improve cardiometabolic health in both animals and humans. Additionally, it has been reported that an early time-restricted diet, in which individuals eat their meals during the daytime and fasting for the rest of the day, improves 24-hour glucose levels, alters lipid metabolism and circadian clock gene expression.⁷⁵ Further studies are needed to understand whether the time-restricted diet is one of the chronotherapeutics interventions which alters clock gene expression and regulates feeding time.

As the main clock in the human body, SCN carries out the control task in regulating our 24-hour biological, psychological, and social rhythm. However, SCN provides data from many internal and external stimuli in the synchronization of the 24-hour rhythm. One of the most prominent external stimuli in adjusting the circadian rhythm is the time of food intake. Disturbances in the time of food intake can lead to circadian disruption. In addition, there is increasing evidence that phase shifts in the circadian rhythm are associated with metabolic disturbances, impulsivity, disordered eating attitudes, and obesity.

Individuals' social activities, cognitive performances, eating time, and especially the sleep-wake cycle differ according to their circadian typology. This typology is called the chronotype and is basically divided into the morning, intermediate, and evening types. It has been observed that evening-type individuals, who go to sleep late, wake up late, and are cognitively active in the evening, experience eating disorder symptoms more than morning-type individuals do. Evening-type individuals are more prone to night eating symptoms, skipping meals, food addiction, and metabolic disorders. Increasing evidence of the relationship between chronodisruption and disordered eating attitudes has highlighted chronotherapeutic approaches in eating disorders. Studies have shown that bulimic eating behaviors and night eating symptoms are reduced in individuals undergoing bright light therapy.

There is a need to increase the use of circadian rhythm-oriented interventions and treatments in disordered eating attitudes and eating disorders and scientific data on this subject. Chronotherapeutic approaches can provide an easy-to-use, inexpensive, tolerable treatment opportunity for people with eating disorder symptoms. Mistimed feeding and disordered eating attitudes are associated with metabolic disorders and obesity, which may suggest that chronotherapeutic approaches are a promising area.

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