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Circadian Rhythm and Adjusting the Diet

Sirkadiyen Ritim ve Beslenme Düzeninin Ayarlanması

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Abstract

The circadian rhythm covers the physiological, biochemical and behavioral effects of the world's light and dark cycles on living things. Food intake time, sleep pattern, melatonin, nutrient content, microbiota affect circadian rhythm genes in peripheral tissues. Intake of food in the wrong circadian ime, poor sleep, constant travel and lack of balanced nutrient intakes cause body weight gain, hypoglycemia, high glucose permeability and impaired activity of hepatic glucose regulatory genes. In order to avoid these metabolic effects, "chrono-nutrition", an emerging branch of chronobiology, states that in addition to the amount and content of food coordinated with the body's daily rhythms, mealtime is critical to the health of an organism and time-restricted nutrition must be present. The aim of this review is to evaluate the other factors affecting the circadian rhythm which is disrupted by current irregular lifestyles, and to evaluate the right nutrition policies and lifestyle changes.

Keywords: Energy regulation, circadian rhythm, sleep pattern, chrono-nutrition

Özet

Sirkadiyen ritim dünyanın aydınlık ve karanlık döngüsünün canlılar üzerinde oluşturduğu fizyolojik, biyokimyasal ve davranışsal etkileri kapsamaktadır. Besin alım zamanı, uyku düzeni, melatonin, besin içeriği, mikrobiyata perifer dokulardaki sirkadiyen ritim genlerine etki etmektedir. Yanlış sirkadiyen zamanda besin alımı, kötü uyku, sürekli seyahat etme ve dengeli besin öğesi alımlarının olmaması vücut ağırlığının artışına, hipoglisemi, yüksek glukoz geçirgenliği ve hepatik glukoz düzenleyici genlerin etkinliğinin bozulmasına sebep olmaktadır. Bu metabolik etkilerin olmaması için gelişmekte olan bir krono biyoloji dalı olan "krono-beslenme" vücudun günlük ritimleriyle koordineli yiyecek miktarı ve içeriğinin olması gerektiğine ek olarak, yemek zamanının da bir organizmanın sağlığı için kritik olduğunu ve zaman kısıtlı beslenmenin olması gerektiğini belirtmektedir. Bu derlemenin amacı günümüzde düzensiz yaşam tarzları ile bozulan sirkadiyen ritme etki eden diğer faktörleri ve doğru beslenme politikalarını ve yaşam tarzı değişikliklerini değerlendirmektir.

Anahtar Kelimeler: Enerji düzenlemesi, sirkadiyen ritim, uyku düzeni, krono-beslenme

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1. Introduction

The word circadian consists of the words “circa” (about) and “dies” (day) and means “about one day”. The circadian rhythm covers the physiological, biochemical and behavioral effects of the light and dark cycle on living things. It enables living organisms, especially mammals, to adapt to environmental changes. Circadian system has the following features:

- A central clock is located in the suprachiasmatic nucleus (SCN) of the hypothalamus.
- It consists of a set of peripheral clocks found in almost all other tissues of the body.

The central clock regulates metabolism, particularly through cortisol, melatonin and synaptic connections. Peripheral tissues integrate these signals from the central clock into their autonomic rhythms to rhythmically regulate metabolism with behavioral and environmental factors (including physical activity, light, sleep and nutrition) (Poggiogalle et al., 2018).

These circadian rhythms have evolved over millions of years to temporarily separate metabolic processes and regulate repetitive feeding-starvation cycles to optimize metabolic efficiency (Poggiogalle et al., 2018). Nutritional behaviors that can affect the circadian rhythm can affect appetite, hunger and satiety, and ghrelin and leptin hormones (Basak et al., 2021). As a result of the disruption in the circadian rhythm, an increase in the hormone leptin and insufficient saturation occur. Uncontrolled hunger leads to excessive energy intake (Oike et al., 2014).

Table 1. Effects of Circadian Rhythm on Human Metabolism

	Circadian Rhythm
Glucose metabolism	
Glucose tolerance	Yes
Fasting glucose	Mixed
Postprandial glucose	Yes
Fasting insulin	No
Postprandial insulin	Mixed
Beta-cell susceptibility	?
Insulin secretion	Yes
Insulin clearance	Yes
Peripheral insulin sensitivity	Yes
Lipid metabolism	
Cholesterol synthesis rate	?
Total cholesterol	?
LDL cholesterol	?
HDL cholesterol	?
Triglycerides	Yes
Free fatty acids	No
Plasma phospholipids	At least some
Plasma acylcarnitines	?
Diglycerides	Yes
Mitochondrial lipid oxidation	?

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Table 1. Effects of Circadian Rhythm on Human Metabolism (continued)

Energy metabolism	
Energy expenditure	Yes
Resting energy expenditure	No
Thermic effect of food	Yes
Fasting Respiratory Coefficient	No
Toughness Respiratory Coefficient	Mixed
Hunger	Yes
Food intake	No

"?" its effect on the circadian system is unknown."Mixed" means that the data is contradictory (Poggiogalle et al., 2018).

For this purpose, the review is planned to evaluate the current approaches in changing the diet and lifestyle due to the factors affecting the circadian rhythm, especially due to recent lifestyle changes.

1.1. Circadian Rhythm and Energy Regulation

The circadian rhythm provides energy homeostasis by controlling glucose and lipid levels in animals and humans (Table 1). For example, it has been reported that 27 out of 159 lipids (~17%) are secreted from the liver and they regulate reaching peak levels during the light phase, thus controlling lipid metabolism and accumulation in the liver (Li et al., 2020). In mammals, BMAL1 (brain and mouse argonaut-like 1) and CLOCK (circadian locomotor output cycles caput) are the 2 main genes involved in regulating their biological functions and circadian gene expression (Kartlaşmış et al., 2017). Impairment of the activation of the BMAL1 gene in the liver causes hypoglycemia, high glucose permeability and impaired activity of hepatic glucose regulatory genes by affecting the fasting phase of the daily nutritional cycle (Li et al., 2020).

As a result of disruption in the circadian rhythm, an increase in the hormone leptin and insufficient saturation occur. Uncontrolled hunger leads to excessive energy intake. Disruption in the circadian clock can cause impaired insulin secretion and hypoinsulinemia. The circadian rhythm-related BMAL1 and CLOCK proteins bind to the distal regions of pancreatic β-cells, resulting in insulin production and release (Oike et al., 2014).

1.2. Factors Affecting Circadian Rhythm

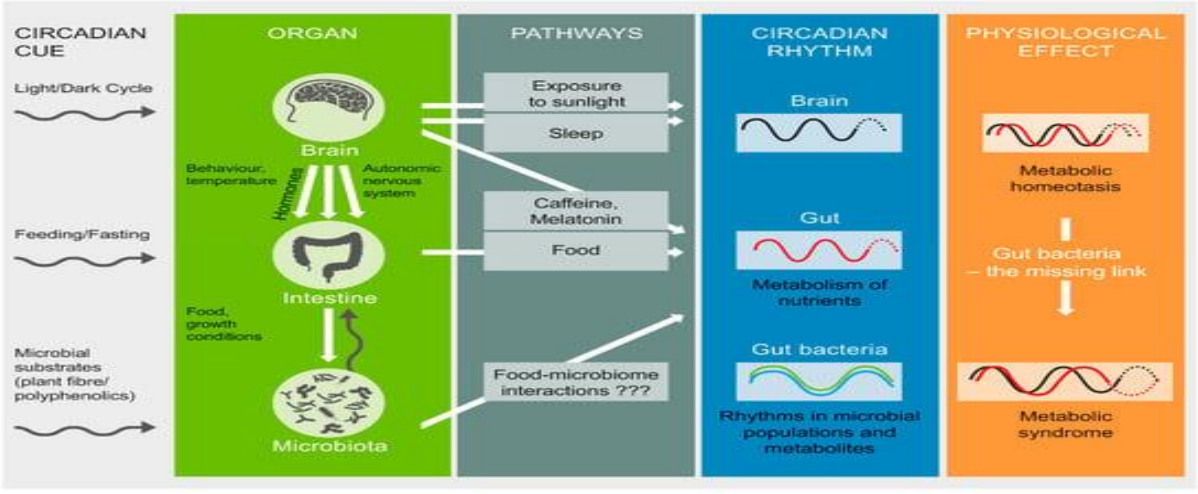

Figure 1. Factors Affecting Circadian Rhythm and Metabolic Effects (Parkar et al., 2017)

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1.2.1. Nutrient Intake Time

Being awake during the night leads to physiological and behavioral disorders because it creates a state of mismatch between the circadian rhythm and the sleep-wake cycle. Circadian rhythm disturbances are common in shift workers, putting them at risk for metabolic syndrome, obesity and diabetes (McHill et al., 2014).

Eating timing affects tissues and different organs related to food absorption, digestion and metabolism, such as stomach, intestine, liver, pancreas or adipose tissue. Environmental clocks are important in food intake, and the timing of eating may be determinant in fat deposition-mobilization and weight loss (Lopez-Minguez et al., 2019).

Spain is one of the countries that eat dinner late in Europe. On average, this time is around 22:00 for the Spaniards, 21:00 for the Italians, 20:00 for the French, 19:00 for the Germans and 18.00 for the Swedes (Lopez-Minguez et al., 2019). An American cohort of 15,000 adults states that for most individuals, this feeding time is 12 hours, and for more than half it reaches 15 hours (Kant et al., 2018). A similar study in India suggests that prolonging the daily feeding period may be a factor in the development of metabolic diseases (Gupta et al., 2017).

With the measurement made in 7 healthy young men using indirect calorimetry; It has been reported that there is a 17% difference in energy expenditure, with the highest values between 9:00 and 12:00 and the lowest values between 00:00 and 06:00. It has been determined that the thermic effect of food is up to 44% higher in the morning than in the afternoon and evening, but there is no difference between morning and afternoon values (Poggiogalle et al., 2018). In another study, it was determined that the resting metabolic rate was 6% higher at noon than in the morning. The mean resting metabolic rate was 1509.7 ± 33.7 kcal/day measured in the morning and 1597.9 ± 32.5 kcal/day measured in the afternoon (Haugen et al., 2003).

In a study conducted with 14 shift workers (individuals sleeping <7 hours or >9.25 hours were not included in the study), total daily energy expenditure increased by 4% on the day of transition to the first night shift after an afternoon nap and prolonged wakefulness, and the second and third night shifts were not included in the study. It was determined that total daily energy expenditure decreased by 3% in one (McHill et al., 2014).

In a similar study, it was determined that shifting the lunch time from 13:00 to 16:30 for 1 week decreased fasting energy expenditure by 4% (Bandin et al., 2015). In another study by Wehrens et al., the effect of a 5-hour delay in meals on peripheral circadian rhythms was investigated. Ten healthy young men were given three meals (breakfast, lunch, and dinner) at 5-hour intervals, starting to eat 0.5 (early) or 5.5 (late) hours after waking. Participants were accustomed to early meals and then switched to late meals for 6 days. There was no change in plasma melatonin and cortisol rhythms. There were no changes in glucose rhythms, melatonin, cortisol plasma insulin and triglyceride rhythms, or clock gene rhythms in whole blood at the end of the study. However, a decrease in plasma glucose concentration following late meals has been observed. (Wehrens et al., 2017).

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In a study conducted to evaluate the role of timing of feeding in body weight loss (79% female) who underwent bariatric surgery; 270 patients were followed for 6 years, individuals were classified according to the timing of the main meal (before or after 15:00) and the study showed that the latter can be an important factor to consider in weight loss treatment even after bariatric surgery. Of the individuals who ate late, ~70% were individuals who lost a little weight. (Ruiz-Lozano et al., 2016). Similarly, in a study conducted with rats, the effects of fructose (10%) intake in the 12-hour light period (07:00-19:00 hours) or the 12-hour dark period (19:00-07:00 hours) were examined. As a result, it was determined that mice given fructose during the light period showed insulin resistance with increased adiposity as well as high insulin and leptin levels. This shows that metabolic activities are higher in the light period. (Morris et al., 2012).

1.2.2. Time Restricted Nutrition

Time-restricted feeding is a form of intermittent fasting that limits daily food consumption to a 4-12 hour period and induces a 12-20 hour fasting interval per day. It is stated that prolonging the daily eating period may contribute to the onset of chronic diseases. It caused an average of 3% weight and fat mass loss after time restriction. This fat loss has also been observed without any calorie restriction. There have been beneficial metabolic effects independent of weight loss, and this is thought to be an intrinsic effect of nutrition based on a reorganization of the circadian clock (Afader et al., 2020). In a study conducted during Ramadan, it was found that the circadian rhythm of body temperature was reversed and there was a significant decrease in mouth temperature at 09:00, 11:00, 13:00 and 16:00 and a significant increase at 23:00 and 00:00 hours. Ramadan fasting has shown that body temperature and hormone secretion delay the circadian rhythm (Qasrawi et al., 2017). In another study, it was determined that time-restricted feeding affected the expression of circadian rhythm genes in mice, reducing weight gain without changes in total energy intake and physical activity level (Chaix et al., 2019).

1.2.3. Sleep patterns

Basically, the sleep-wake cycle is one of the important regulators of the circadian rhythm. However, working 24/7 in the modern world and the widespread use of television, internet and mobile phones lead to a gradual decrease in adequate sleep time. An epidemiological study reports that nighttime sleep time has decreased by 18 minutes over the past 30 years. (Kronholm et al., 2008; Serin et al., 2019).

Melatonin is an important hormone in the circadian rhythm. At night, melatonin synthesis and release are stimulated in the dark, while during the day they are suppressed by light. Especially between 23:00 and 05:00, melatonin secretion peaks 3-10 times. However, exposure to light at night causes a decrease in plasma melatonin levels. (Serin et al., 2019). Similar trends in increased melatonin suppression and delayed circadian rhythm, reduced evening sleepiness, and increased morning sleep have been reported recently with the use of unrestricted light-emitting devices. The states that the reason for this is that melanopsin receptors are more sensitive in the evening and at night, and most of the sleep disorders may be related to low blue light exposure just before going to bed at night.

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(Amanpour et al., 2021). Especially in healthy individuals, disruption of the sleep-wake cycle causes premature death, obesity, diabetes, anxiety, impaired glucose tolerance, depression and progression of cancer. It is stated that working at least 3 nights a month for 15 or more years may increase the risk of colorectal cancer in women (Schernhammer et al., 2003). In another study, the insulin sensitivity of adipocytes after a short sleep period was found to be 30% less than the insulin sensitivity of adipocytes after a normal sleep period (Hernández-García et al., 2019).

1.2.4. Nutritional Content

The ratio of nutrients in the diet has important effects on circadian clocks, especially by affecting circadian rhythm genes in peripheral tissues (Li et al., 2020). In a controlled study with rats, it was reported that a diet containing 45% carbohydrates, 20% protein and 35% fat for 11 months changed the circadian clock genes in the liver and kidneys that cause obesity (Hesieh et al., 2010). Similarly, in a study conducted with rats, it was determined that giving a 60% fat diet for 10 weeks completely blocked the release of nicotinamide adenine dinucleotide (NAD +) and had a negative effect on the energy balance (Eckel-Mahan et al., 2013).

A cross-controlled study on 10 healthy men showed an increase in body temperature and suppression of melatonin production and a shift in the circadian clock after a carbohydrate-rich dinner for 3 consecutive days (Burke et al., 2011). However, a higher glucose tolerance in the morning indicates that carbohydrate intake in the early hours is more accurate (Johnston, 2014).

In addition, some B vitamins are directly or indirectly linked to circadian rhythms and sleep patterns (Parkar et al., 2019). This is related to the daily endogenous circadian rhythmicity of vasopressin. However, a positive psychotropic stimulating effect of vitamin B-12 was found against the tendency to reduce sleep in the sleep-wake cycle (Beydoun et al., 2014).

In addition, naturally occurring polyphenols in plants not only have a wide range of beneficial effects for human health, but also act as modulators of the circadian clock in vivo. Polyphenols include compounds such as polyphenolic amides, flavonoids and phenolic acids that can be found in food products, especially spices, herbs, fruits, nuts and seeds. Although their effects on circadian rhythm are not limited to adipose tissue, resveratrol, proanthocyanidins and epigallocatechin gallate have also been found to affect body weight and fat mass reduction (Ribas-Latre et al., 2022).

1.3. Gut Microbiota as a Potential Way to Improve Circadian Rhythm

It has long been known that the function of the gastrointestinal tract has circadian rhythms, but emerging data indicates that the microbiome also has diurnal changes. It shows that the number and type of bacteria in the epithelial mucus layer varies between light and dark periods and is closely related to the circadian rhythm, although the mechanisms are still not understood (Bishehsari et al., 2020). Table 2 shows the microorganism species and their effects on the circadian rhythm. Therefore, regulating the microbiome is seen as a promising strategy for restoring the host's circadian rhythm and metabolic homeostasis. Plant sources are very rich in polyphenols. The indigestible components reach the colon and produce beneficial metabolites, including short-chain fatty acids and polyphenolic

bioactives, which not only help maintain colon health but also resynchronize circadian rhythms. (Parkar et al., 2019).

Table 2. Circadian Rhythm and Microbiota Mediated Mechanisms Influencing Metabolic Pathways

Microorganisms	Microbial Function
Firmicutes (Lachnospiraceae, Erysepelotrichaceae, Clostridiaceae Ruminococcaceae, *Lactobacillus*), *Bifidobacterium* and Bacteroidetes	Microbial bile salt hydrolases deconjugate bile lithocholic acid and deoxycholic acid.
Bilophila wadsworthia, Desulfovibrio, Desulfobulbus, Desulfotobacter	It produces hydrogen sulfide in the colon.
Lachnospiraceae*, Eubacterium rectale*, and *Ruminococcus bromii, Faecalibacterium prausnitzii*	Breaks down dietary fiber to produce butyrate in the colon.
Ruminococcus gnavus and Clostridum sporogenes	Produces biological amines such as serotonin

(Parkar et al., 2019)

1.4. Chrono-nutrition

The urban environment has changed drastically in the last decades, and this has had an impact on sleep and diet patterns and chronic diseases. In parallel, dietary patterns and lifestyles are changing, including more shift work, more meals outside or more disordered eating habits, including eating late at night and skipping breakfast. For example, more than half of the best-selling drugs in the United States target circadian genes, and more than 100 of the World Health Organization's essential drugs act on circadian genes (Kuhlman et al., 2018).

Chrono-nutrition is an emerging branch of chronobiology that focuses on the profound interactions between metabolism and biological rhythms. This framework shows that alongside all biological processes, even nutrition follows a circadian pattern (Masi et al., 2022). It covers energy distribution, meal frequency and pattern, duration of the eating period and the relative importance of these factors for metabolic health and risk of chronic disease (Flanagan et al., 2021).

2. Conclusion

The circadian rhythm is strongly linked to metabolic balance and contributes to the maintenance of both central and peripheral clocks. Widespread use of artificial light in modern lifestyle, long working hours, widespread social activities and industrialization that can travel rapidly between time zones cause disruption of internal circadian rhythms. Disruption of the rhythm causes increased cardiovascular diseases and metabolic diseases, including cancer. Nutrition is an important factor in the regulation of circadian rhythm. Low food intake at night, balanced intake of nutrients, and time-limited eating patterns should be made a lifestyle. For melatonin secretion, one should not sleep too late and in bright environments. Since the number and variety of beneficial bacteria in the microbiota can affect the circadian rhythm, food sources and probiotics that can increase the number of beneficial bacteria in the flora can be used.

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Conflict of Interest

There is no conflict of interest.

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