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Review Article

The impact of chrononutrition on metabolic health: Aligning eating patterns with circadian rhythms

Seema Lekhwani[1]*, Narain Das Vaswani[2]

[1]Dept. of Biochemistry, Pt. B. D. Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India
[2]Dept. of Pediatrics, Pt. B. D. Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India

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ABSTRACT

Chrononutrition, the study of how the timing of meals impacts health by aligning with the body's circadian rhythms, is increasingly recognized for its influence on metabolic regulation. This review examines the scientific foundation of chrononutrition, focusing on key research surrounding meal timing, circadian disruption, and their effects on metabolic disorders such as obesity and type 2 diabetes. Findings from both clinical trials and animal studies indicate that irregular eating schedules can disturb circadian rhythms, resulting in impaired glucose metabolism, increased fat accumulation, and hormonal imbalances. This review also identifies critical gaps in the current research, highlighting the potential for chrononutrition-based strategies in preventing and managing disease.

1. Introduction

Chrononutrition is an emerging interdisciplinary field that explores how the timing of food intake influences metabolic health by aligning with the body's natural circadian rhythms. Traditionally, dietary research has primarily focused on macronutrient composition, caloric intake, and the balance of protein, carbohydrates, and fats. While these factors are undoubtedly crucial for health, growing evidence indicates that the timing of food intake may be just as important as what and how much we eat in determining health outcomes.[1]

The circadian rhythm, which is the body's 24-hour internal clock, is controlled by the suprachiasmatic nucleus(SCN) in the hypothalamus.[2] This clock synchronizes physiological functions—including hormone secretion, sleep-wake cycles, and energy metabolism—to align with the light-dark cycle. Circadian rhythms optimize processes like glucose metabolism in the morning, when the body's insulin sensitivity is highest, and promote energy storage later in the day.[3]

Modern lifestyles, however, often involve disruptions to natural circadian rhythms, primarily due to irregular meal timings, shift work, and nighttime eating**.** This misalignment between our internal clock and external behavior is termed chronodisruption. Research suggests that chronodisruption—especially in cases of erratic eating patterns—can lead to metabolic dysfunctions, including obesity, insulin resistance, and type 2 diabetes.[4]

Furthermore, as shift work becomes increasingly common, with workers being required to eat and sleep at circadian misaligned times, the need to address the relationship between meal timing and metabolic health grows ever more urgent.[5] This review will explore how chrononutrition interventions, such as time-restricted feeding(TRF) and intermittent fasting(IF), have the potential to realign meal timing with the body's biological clock, improving metabolic health outcomes in

* *Corresponding author*.
E-mail address: s_lekhwani@yahoo.co.in (S. Lekhwani).

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both humans and animals.

1.1. The role of circadian rhythms in metabolism

The body's circadian rhythms govern a wide range of metabolic processes, ensuring that biological functions occur at the most efficient times during a 24-hour period. These rhythms control when we are most alert, when our body is best at digesting food, and when we should sleep or conserve energy. Importantly, they also regulate insulin sensitivity, glucose metabolism, and energy storage. Central to the circadian system is the suprachiasmatic nucleus(SCN), located in the hypothalamus, which functions as the body's master clock.[6] The SCN synchronizes circadian rhythms with external environmental cues, such as light exposure and meal timing.

The circadian system is not solely governed by the SCN; there are also peripheral clocks located in organs such as the liver, pancreas, muscles, and adipose tissue. These peripheral clocks help regulate tissue-specific metabolic functions. For instance:

1. The liver's clock plays a key role in controlling glucose production and insulin sensitivity throughout the day.
2. The pancreas regulates insulin release, while adipose tissue controls fat storage and energy balance.[7]

When feeding schedules align with the body's circadian rhythms—such as eating earlier in the day when insulin sensitivity is higher—metabolic homeostasis is maintained. In contrast, misalignment between circadian rhythms and eating patterns, such as consuming large meals late at night, can disrupt these processes, leading to metabolic disorders like obesity and type 2 diabetes.[8]

Animal studies further support this, showing that mice fed during their inactive phase(the mouse equivalent of human nighttime eating) develop obesity, insulin resistance, and metabolic syndrome, even when their caloric intake is kept constant.[9] These findings emphasize the importance of meal timing and its synchronization with the body's natural metabolic rhythms.

1.2. Circadian disruption and metabolic disorders

Circadian disruption occurs when there is a misalignment between the body's internal clock and external behaviors, such as irregular sleep patterns, shift work, or eating at non-optimal times. The metabolic processes regulated by circadian rhythms, such as insulin sensitivity, glucose metabolism, and energy storage, are all affected when these rhythms are disrupted. The result is an increased risk of developing metabolic disorders, including obesity, type 2 diabetes, and metabolic syndrome.

1.2.1. Human studies

In a 2014 study by Leproult et al. researchers found that circadian misalignment—caused by shifting sleep and meal times outside of normal circadian patterns—led to increased insulin resistance, inflammation, and elevated levels of cortisol.[4] These findings are particularly relevant because insulin resistance is one of the earliest markers of metabolic syndrome, and chronic inflammation is a known risk factor for cardiovascular disease.

A study by Scheer et al.(2009) analyzed the health of shift workers, who often eat meals during times of circadian misalignment. The research showed that shift workers are at a significantly higher risk of developing obesity, insulin resistance, and type 2 diabetes due to their disrupted meal patterns, which conflict with their natural biological clocks.[7]

1.2.2. Animal studies

In a notable study by Turek et al.(2005), mice with mutations in key circadian clock genes developed metabolic syndrome, marked by insulin resistance, obesity, and dyslipidemia.[10] Another animal study demonstrated that when mice were fed during their inactive phase(similar to nighttime eating in humans), they exhibited significant weight gain and impaired glucose tolerance—even when caloric intake was controlled.[11] These results suggest that circadian disruption plays a fundamental role in the onset of metabolic disorders, independent of calorie consumption.

1.3. Chrononutrition interventions

1.3.1. Time-restricted feeding(TRF) and intermittent fasting(IF)

1. Time-Restricted Feeding(TRF) involves restricting food intake to a specific window of time each day, typically between 8 and 12 hours, while fasting for the remaining hours. Unlike other forms of fasting, TRF does not necessarily reduce calorie intake but rather limits the hours during which food is consumed. TRF is designed to align food intake with the body's circadian rhythms, taking advantage of the natural peaks in metabolic efficiency. Studies show that when food is consumed earlier in the day—during the periods of peak insulin sensitivity—metabolic outcomes improve (Table 1).[12]
2. Intermittent Fasting(IF), on the other hand, alternates between periods of eating and fasting over longer intervals. Common IF patterns include the 16:8 diet(16 hours of fasting and an 8-hour eating window) or the 5:2 diet(normal eating for five days and severe caloric restriction for two days). Like TRF, IF is hypothesized to work through the synchronization of food intake with metabolic activity regulated by circadian rhythms, but it also promotes metabolic flexibility by encouraging the body to switch between

fat and glucose as fuel sources during the fasting periods (Table 2).[13]

1.4. Mechanisms of TRF and IF within chrononutrition

1. TRF aligns food intake with periods of peak insulin sensitivity and glucose metabolism, which occur in the morning and early afternoon. Eating during these hours enhances glucose tolerance and reduces fat storage, as the body is more efficient in processing food during this time. Studies indicate that early TRF(where all meals are consumed within a 6-8 hour window, typically finishing by mid-afternoon) can improve insulin sensitivity, blood pressure, and markers of oxidative stress—even without weight loss.[14]
2. IF works by extending the natural overnight fasting period. It enhances metabolic flexibility, allowing the body to switch from using glucose as its primary fuel source to utilizing fat stores. This transition, also known as ketosis, improves fat oxidation and insulin sensitivity. IF has also been linked to reductions in inflammatory markers and improvements in blood lipid profiles. Studies on humans and animals show that IF can protect against diet-induced obesity, diabetes, and other metabolic disorders.[15]

1.5. Human and animal studies supporting TRF and IF

1.5.1. Animal studies

1. In a study conducted on mice, it was shown that time-restricted feeding of a high-fat diet resulted in significant improvements in glucose metabolism, insulin sensitivity, and reduced fat accumulation when compared to mice that were allowed to eat the same diet at any time(Table 1).[16] The mice subjected to time-restricted feeding were also protected from obesity and type 2 diabetes, which suggests that aligning feeding with circadian rhythms can profoundly affect metabolic health.
2. Another animal study demonstrated that intermittent fasting could reduce weight gain, improve fat oxidation, and enhance insulin sensitivity even without caloric restriction. This indicates that when food is eaten, rather than how much, plays a crucial role in metabolic regulation(Table 2).[17]

1.5.2. Human studies

1. A clinical trial on early time-restricted feeding(eTRF) showed significant health benefits, including improved insulin sensitivity, lower blood pressure, and reduced oxidative stress, even in the absence of significant weight loss. Participants in this study ate between 8 a.m. and 2 p.m. and fasted for the remainder of the day, illustrating the importance of meal timing in metabolic health (Table 1).[18]
2. In a separate study on intermittent fasting, overweight participants following a 5:2 fasting regimen experienced a significant reduction in body fat, improved insulin sensitivity, and lower levels of inflammatory markers. This supports the hypothesis that intermittent fasting promotes metabolic flexibility and improves overall health outcomes(Table 2).[19]

2. Discussion

As the field of chrononutrition advances, it has become increasingly clear that meal timing plays a pivotal role in metabolic health. Circadian rhythms are not only responsible for regulating sleep-wake cycles but also play a central role in glucose metabolism, insulin sensitivity, and fat storage. Disruptions to these rhythms—whether through shift work, late-night eating, or irregular meal timing—are strongly linked to the development of metabolic disorders such as obesity, type 2 diabetes, and metabolic syndrome.

Time-Restricted Feeding(TRF) and Intermittent Fasting(IF) have emerged as promising chrononutrition interventions that align food intake with the body's natural metabolic rhythms. TRF limits food intake to specific time windows, typically during periods of peak insulin sensitivity, while IF alternates between periods of fasting and feeding, allowing the body to enter a state of metabolic flexibility, where it shifts from glucose to fat as its primary fuel source. Human and animal studies show that these interventions not only improve insulin sensitivity but also reduce inflammation, fat accumulation, and oxidative stress (Tables 1 and 2).

Importantly, shift workers and individuals with erratic eating patterns stand to benefit the most from chrononutrition interventions, as realigning their eating habits with their circadian rhythms could significantly reduce their risk of developing metabolic diseases. Long-term human trials are still needed to fully understand the long-term effects of TRF and IF across different populations, but the current evidence suggests that these interventions could be integrated into public health strategies for the prevention and management of metabolic disorders.

3. Conclusion

The growing body of research on chrononutrition highlights the critical role that meal timing plays in regulating metabolic health. By aligning food intake with circadian rhythms, interventions like time-restricted feeding(TRF) and intermittent fasting(IF) can optimize metabolic processes, improving insulin sensitivity and glucose metabolism and reducing fat accumulation.

Research shows that circadian disruption, caused by shift work or irregular eating patterns, significantly increases the risk of metabolic disorders such as obesity and type

Table 1: Mechanisms and outcomes of TRF and IF inchrononutrition

Intervention	Mechanism	Human/Animal Study	Outcomes	
Time-Restricted Feeding (TRF)	Aligns eating with circadian rhythms, peaks insulin sensitivity	Human (eTRF study)	Improved insulin sensitivity, reduced oxidative stress, lower	14, 18
Intermittent Fasting (IF)	Enhances metabolic flexibility, switches to fat metabolism	Human (5:2 diet study)	Reduced body fat, improved insulin sensitivity, lower inflammatory markers	19
TRF in High-Fat Diet Mice	Restricts feeding to a specific time window, limits fat storage	Animal (Mice on high-fat diet)	Reduced obesity, improved glucose metabolism, increased insulin sensitivity	16
IF in Obesity-Induced Mice	Promotes fat oxidation, metabolic flexibility during fasting	Animal (Intermittent fasting study in mice)	Reduced weight gain, improved fat oxidation, improved insulin sensitivity	17

Table 2: Human studies on time-restricted feeding and intermittent fasting

Study	Intervention	Participants	Duration	Outcomes	
Sutton et al.(2018)	Early Time-Restricted Feeding (eTRF)	15 overweight men	5 weeks	Improved insulin sensitivity, reduced oxidative stress, lower BP	18
Jakubowicz et al. (2013)	High-Caloric Breakfast	93 obese women	12 weeks	Improved weight loss, better glycemic control	5
Patterson et al. (2015)	Intermittent Fasting (5:2)	107 overweight adults	6 months	Reduced body fat, improved insulin sensitivity, lower inflammatory markers	15

2 diabetes. Studies conducted in both human and animal models have demonstrated the profound effects of meal timing on metabolism, with early TRF and IF emerging as promising interventions for mitigating these risks.

However, more long-term studies are needed to fully understand the sustainability and effectiveness of these interventions across different populations. Furthermore, personalized approaches that consider individual circadian rhythms, genetics, and lifestyle factors are likely to yield the best health outcomes.

As modern lifestyles continue to disrupt natural circadian rhythms, integrating chrononutrition strategies into public health guidelines offers an innovative and scientifically backed approach to improving metabolic health and reducing the global burden of metabolic diseases.

4. Source of Funding

None.

5. Conflict of Interest

None.

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Author biography

Seema Lekhwani, Associate Professor https://orcid.org/0000-0002-0025-9448

Narain Das Vaswani, Professor https://orcid.org/0000-0002-7773-3478

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