# A Systematic Review of Fasting Biology

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## ABSTRACT

Fasting is the pattern-based restriction of nutrient consumption or calories regularly practiced for health benefits. Through fasting, the availability of nutrients depletes and multiple biological responses are triggered. Biological processes that have been observed to respond to nutrient limitation as a result of fasting include: autophagy, glucose regulation, hormone regulation, and circadian rhythm. Although fasting has been implicated to rewire biological processes in the human body, it remains unclear whether fasting has any beneficial health implications. Knowing the full effects of fasting can provide insight on human biological systems and solidify the potential of utilizing fasting as a non-invasive preventive measure for human disease. In this review, we highlight the biological processes fasting affects, and utilizing the research articles we have concluded that fasting is a largely beneficial practice but more clinical studies need to be done to solidify conclusions.

## INTRODUCTION

Fasting, a practice rooted in ancient traditions, refers to a pattern-based restriction of nutrient consumption or calories, and its significance has endured through the ages. In the modern world, fasting has not only retained its religious and spiritual connotations but has also witnessed a surge in popularity due to increasing trends from the fitness industry. Religious fasting has long been observed as a means of purification and discipline, with various faiths incorporating fasting into their rituals as a means of spiritual growth and reflection. Additionally, the contemporary rise in intermittent fasting and time-restricted eating has piqued interest for its potential benefits in weight management and overall well-being. Amidst these assumptions surrounding fasting, it is crucial to delve into its potential impact on health and wellness. Proponents argue that controlled fasting can improve metabolic health, promote cellular repair, and facilitate weight loss. However, as with any dietary practice, fasting necessitates a careful balance, consistency, and moderation to ensure it remains a sustainable and safe lifestyle choice. (1) Understanding the major physiological changes fasting triggers within the body, such as fluctuations in glucose metabolism and hormonal regulation in response to nutrient availability, is essential in making informed decisions about adopting fasting as part of an individual's wellness routine. By exploring these aspects of fasting, we can discern its place in contemporary lifestyles and its potential contribution to personal health and vitality.

### The Biology of Fasting:

Fasting practices initiate immense physiological changes in the human body including; glucose levels, hormones, and cellular processes. Here, I highlight the most pivotal biological modulations in response to fasting.

(2) Glucose, often referred to as the body's primary source of energy, plays a central role in the biology of fasting. During fasting periods, when the intake of food is very limited or absent,

the body undergoes a series of physiological changes to ensure the maintenance of essential functions and energy supply.

In the early stages of fasting, the body's immediate source of glucose comes from the glycogen stores found primarily in the liver and muscles. Glycogen is a stored form of glucose that can be quickly broken down into glucose molecules to provide energy to various tissues and organs. As fasting continues, glycogen reserves become depleted, prompting the body to turn to alternative sources to sustain energy levels.

(3) One crucial adaptation during fasting involves the production of glucose through a process called gluconeogenesis. In this process, the liver synthesizes glucose from non-carbohydrate sources, such as amino acids and glycerol derived from the breakdown of proteins and fats. This newly generated glucose is then released into the bloodstream to fuel the brain, red blood cells, and other glucose-dependent tissues that require a continuous supply of energy.

The interplay between glycogen stores and gluconeogenesis demonstrates the body's remarkable ability to adapt to the challenges of fasting. This intricate web of processes ensures that glucose, a vital fuel for various physiological functions, remains available even in the absence of immediate dietary sources. Understanding the role of glucose in the biology of fasting provides insight into the body's mechanisms for energy conservation and maintenance during periods of healthy fasting.

**Autophagy:**

(4) Autophagy, a cellular process with great implications for health and longevity, is also closely intertwined with the biology of fasting. The actual term "autophagy" originates from the Greek words "auto," meaning self, and "phagy," meaning eating, reflecting autophagy's purpose of self-digestion and recycling within cells. Fasting triggers autophagy as part of the body's response to a lack of nutrients. Autophagy plays a pivotal role in maintaining cellular health, removing damaged components, and adapting to the challenges of fasting.

During fasting, when the body's nutrient intake is limited, cells activate autophagy as a survival strategy. The primary goal of autophagy is to break down and recycle dysfunctional cellular components, such as damaged organelles, to generate amino acids and other building blocks that can be used for energy production and other essential cellular functions. By reusing these damaged components, cells can sustain their basic activities even when external nutrient sources, like food during fasting, are scarce. The process of autophagy involves the formation of specialized structures called autophagosomes, which encapsulate the targeted cellular materials. These autophagosomes then fuse with lysosomes, organelles containing digestive enzymes, resulting in the degradation and recycling of their contents.

(5) The connection between autophagy and fasting extends beyond cellular maintenance. Research suggests that autophagy's activation during fasting may have broader health benefits. It has been implicated in supporting metabolic flexibility, improving insulin sensitivity, and aiding in the removal of toxic substances from cells. Moreover, the link between autophagy and longevity has led to increased interest in its potential role in promoting healthy aging.

As a result, the biology of fasting is intricately intertwined with autophagy, as fasting acts as a potent stimulus for autophagic processes. While some level of autophagy occurs even under normal physiological conditions, fasting and nutrient deprivation amplify this process, enabling cells to adapt, survive, and potentially thrive in the face of adversity. Research into the connections between autophagy and fasting continues to shed light on how these mechanisms impact health, disease prevention, and the overall biology of the human body.

**Circadian Rhythm:**

(6) Circadian biology, the study of biological rhythms and their synchronization with the natural day-night cycle, intersects with the biology of fasting in various ways. Their interaction has profound implications for health, metabolism, and overall well-being. The body's internal circadian clock, often referred to as the "biological clock," conducts a wide array of physiological functions according to a 24-hour cycle. This internal timing system influences processes like sleep-wake patterns, hormone secretion, metabolism, and even cellular repair and maintenance. Fasting, particularly time-restricted eating (like Ramadan, only able to eat when the sun is down) involves limiting food intake to specific time windows, which heavily aligns with circadian rhythms. This practice capitalizes on the natural synchronization between the internal clock and metabolic processes. Emerging research suggests that aligning eating patterns with the circadian rhythm may enhance the body's ability to process nutrients efficiently and promote optimal metabolic health.

When food is consumed during periods of heightened insulin sensitivity (such as daytime for humans), the body is more effective at managing blood sugar levels and utilizing nutrients for energy, as insulin's effects are more potent. Moreover, certain metabolic pathways, including those involved in nutrient absorption, energy expenditure, and fat metabolism, are under the circadian control. Fasting during appropriate times will enhance the alignment of these pathways with the body's natural rhythms, improving metabolic outcomes.

Furthermore, the interaction between circadian biology and fasting goes beyond metabolism. Circadian rhythms also influence autophagy, the process we covered before. Autophagy is the cellular process of self-renewal and maintenance, which is notably activated during fasting. (7) Research suggests that autophagy also exhibits circadian oscillations, with certain aspects of autophagic activity peaking during specific times of the day. Aligning fasting practices with these rhythms optimize the effectiveness of autophagy and cellular repair. In essence, the timing of fasting can influence how the body responds to nutrient intake, energy utilization, and cellular maintenance, all of which are interconnected with circadian rhythms. Combining circadian biology with fasting strategies could potentially amplify the benefits of both approaches, leading to improved metabolic health, better weight management, and enhanced overall wellness.

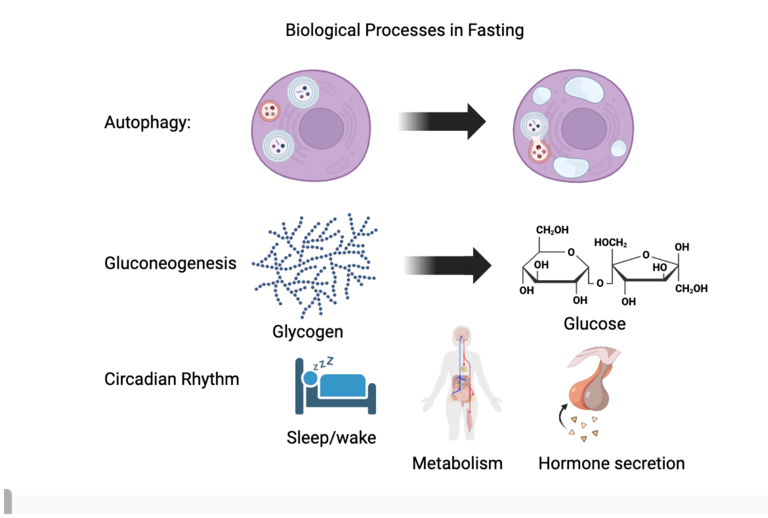


Fig 1: Key biological processes responsive to time-restricted eating

**Hormones:**

(8) Finally, hormones, intricate chemical messengers that regulate various physiological processes within the body, also play a crucial role in the biology of fasting. They orchestrate responses to changes in nutrient availability, helping to maintain energy balance, manage hunger, and sustain stamina during periods of food deprivation/fasting. The interaction between hormones and fasting is a complex system that ensures the body's survival and adapts to different nutritional conditions.

(10) Ghrelin is often referred to as the "hunger hormone" because it stimulates appetite and increases food intake. During fasting or periods of reduced caloric intake, ghrelin levels typically increase, sending signals to the brain that trigger hunger sensations. This evolutionary adaptation encourages individuals to seek out and consume food, helping to ensure an adequate energy supply.

(10) In contrast, satiety hormones work to suppress hunger and promote feelings of fullness. Leptin, produced by fat cells, is a key satiety hormone. Its levels rise as fat stores increase, signaling to the brain that energy reserves are sufficient. However, during fasting or weight loss, reduced leptin levels can lead to increased hunger and a decreased feeling of fullness, potentially making it more challenging to maintain caloric deficits.

(11) During fasting, the body relies on stamina hormones to maintain energy levels and support physical endurance. Adrenaline, also known as epinephrine, is a stress hormone released in response to various stimuli, including fasting. Adrenaline mobilizes stored energy by increasing the breakdown of glycogen and promoting the release of fatty acids from adipose tissue. This process ensures that the body has an available energy source to meet immediate demands.

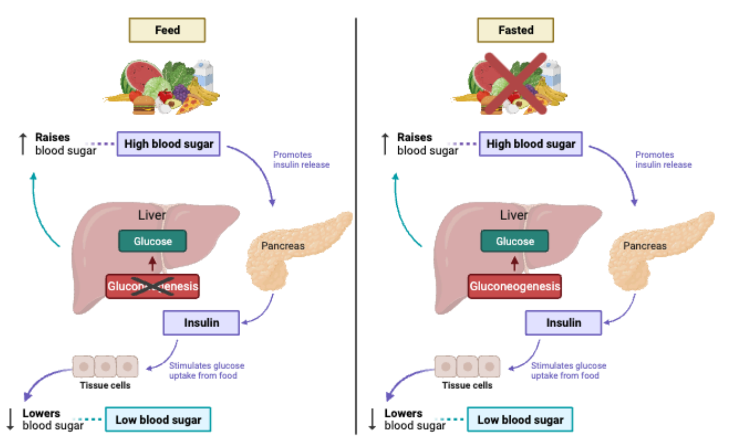


Fig 2: Insulin regulation and response to time-restricted feeding.



(12) Insulin and Glucagon: Insulin and glucagon, hormones produced by the pancreas, work together to regulate blood glucose levels. When fasting, insulin levels decrease, allowing the body to conserve glucose for vital functions. Conversely, glucagon is released, promoting the breakdown of glycogen into glucose to maintain blood sugar levels. This hormonal interplay helps prevent dangerous blood sugar fluctuations during periods of fasting.

Hormones are integral to the biology of fasting, orchestrating a response to changes in nutrient availability. They regulate hunger and satiety cues, help maintain energy levels through the mobilization of stored nutrients, and ensure the body's survival and function during fasting periods. Understanding how these hormones interact with fasting can provide insights into the body's adaptations to different nutritional conditions and inform strategies for optimizing health.

**Potential of using Fasting as an intervention:**

The interplay of fasting and primary health outcomes remain largely uncovered. Studies over the last couple of years have observed various health parameters and time-restricted feedings to provide insight into this interplay. A 2021 study from the University of Illinois at Chicago subjected obese individuals to time-restricted feedings and monitored sleep quality, degree of insomnia, and sleep apnea. After 8 weeks of time-restricted feedings, they concluded there was no difference in the time-restricted fed group and their respective control group. In tandem, the same UIC researchers performed a similar study across a longer duration of 12 weeks, and still did not see any difference in overall sleep health. A 2018 study from the University of California, San Francisco and the University of Hawai'i Cancer Center investigated the overall metabolic effects of 16hr time-restricted eating on overweight and obese individuals. The 12-week study determined that time-restricted eating did indeed decrease an individual's body weight; however, the control group also observed a very modest decrease in body weight. Neither group saw any differences in fat mass, lean mass, insulin, glucose, and hemoglobin levels. The authors concluded that there is no additional benefit in time-restricted eating as compared to normal non-restricted eating for losing body weight. In sharp contrast, the University of California, San Diego Division of Cardiovascular Diseases conducted a study of 10hr time-restricted eating for individuals with metabolic disorders. For the 12-week study, the authors concluded that this TRE intervention improves cardiometabolic health for individuals with metabolic syndrome with lowering blood pressure, inflammation markers, and overall body weight while changing lipid profiles.

**Health and Fasting**

(13)Studies have indicated that intermittent fasting can lead to improvements in insulin sensitivity, blood sugar levels, and weight management. This approach may help reduce the risk of type 2 diabetes and obesity-related health diseases. (14) Fasting has also been associated with improvements in cardiovascular risk factors such as blood pressure, cholesterol levels, and inflammation. These improvements could contribute to a reduced risk of heart disease. For cancer prevention and treatment, research suggests that fasting could potentially enhance the body's ability to fight cancer cells while protecting healthy cells. Fasting might also improve the effectiveness of certain cancer therapies. For neurological health, fasting has shown promise in promoting brain health by supporting neuroplasticity, reducing oxidative stress, and possibly reducing the risk of neurodegenerative disorders such as Alzheimer's and Parkinson's disease.

**CONCLUSION**

In conclusion, fasting is a concept deeply rooted in history and culture, but it has also found a new place in the modern world as a healthy method of cleansing and preventing illnesses. Throughout this review, we've explored the biology of fasting, examining its effects on glucose levels, autophagy, circadian rhythms, and hormonal regulation. These intricate biological changes underscore the importance of understanding fasting's impact on the body. As a Buddhist, and someone who has personally experienced fasting on a weekly basis in a religious context, I can attest to the exemplary benefits of fasting as a tool for weight loss, an improvement in cardiovascular health, and how it makes me feel and become a healthier person overall. However, there's a profound contrast between fasting's role in my own life and that of many individuals in Western culture. In the fast-paced Western world, where food is often abundant and accessible, the necessity for fasting is less prevalent, and therefore the benefits are overlooked. However, the increasing trends in intermittent fasting and other dietary practices suggest a shifting positive cultural attitude toward fasting as a tool for health and wellness. Clinical studies have played a pivotal role in compiling this research, shedding light on how fasting can positively influence various parameters like blood glucose levels and hormone regulation which results in clear benefits such as improved insulin sensitivity and reduced inflammation. Yet, much work remains to be done to solidify these conclusions. Further research is needed to better understand the long-term effects of fasting, its suitability for different individuals, and its potential risks. While fasting may hold promise for many, it's crucial to approach it with a balanced and informed perspective. In my opinion, fasting is a positive practice that should be undertaken, in a consistent and controlled manner, for healthy long-term benefits. Ultimately, this review has provided an overview of the science and cultural aspects of fasting, offering valuable insights into its potential benefits, but it is important to consult with healthcare professionals and consider personal circumstances before making any significant changes to one's dietary habits.

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