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Original article

Fasting and Its Impact on Microbiota, Metabolism, and Well-Being: A Physiological and Nutritional Approach

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Abstract

The modern lifestyle, characterized by uncontrolled eating, fast rhythm and lack of regular periods of metabolic rest, has significantly influenced the increase in chronic morbidity and the destabilization of the intestinal microbiota. Together with environmental pollution and constant stress, these factors have contributed to the deterioration of the population's health, prompting the search for natural and effective alternatives for rehabilitation. Fasting, known for centuries as a spiritual and physiological practice, has gained increasing interest in recent decades as a possible strategy for metabolic regeneration, increasing insulin sensitivity, stimulating autophagy and significantly improving the intestinal microbiota. Numerous studies at the global level in animal and human models clearly demonstrate the potential of fasting for cell regeneration, reducing inflammation and increasing the body's protective capacities. The aim of this study is to investigate the impact of fasting on the remodeling of thegut microbiota and the improvement of metabolic and mental functions. Special attention is givento the distinction between the microbiota inherited at birth and the one gradually shaped throughout life by nutrition and lifestyle. The analysis is structured around a theoretical framework developed step bystep, unraveling the biological mechanisms triggered during fasting and their effects onthegut microbiota. A multidisciplinary perspective is adopted, incorporating insights on autophagy, stem cells, ketone body production, and refeeding phases in relation to the intestinal flora. Complementary laboratory data are included, primarily from the scientific literature, alongsideselected original food analyses. These are not only for their nutritional value alone, but tobetterunderstand how specific foods promote or hinder the growth of beneficial gut microbe. Fasting, through temporary suspension of food intake, activatesmetabolic pathways that support the regeneration of the gut microbiota and enhance insulinsensitivity. Reduced oxidative stress, increased mental clarity, and a more stable microbial composition were observed. Fasting represents a natural and controlled mechanism for rebalancing the body–microbiota relationship, offering significant benefits for metabolism, cognition, and long-termwell-being.When applied carefully and adapted to individual needs, it can serve as a powerful preventive and supportive health strategy.

Keywords: Fasting, Microbiota, Metabolism, Refeeding, Well-Being.

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INTRODUCTION

Definition and Types of Fasting

Fasting, in its broadest sense, is a conscious and temporary abstention from food, liquids, or both. From a biological perspective, it acts as a regulatory signal for the body that activates reparative and restructuring processes (Longo & Panda, 2016).

For the organism, the absence of food is not an extraordinary stressor, but an evolutionary stimulus that triggers beneficial metabolic pathways such as autophagy, ketogenesis, immune regeneration and hormonal control (de Cabo & Mattson, 2019).

Types of fasting

Intermittent fasting – This fasting involves daily or weekly alternations between periods of eating and abstinence. The most common formats are 16:8, 5:2 or a 24-hour fast once per week. It is associated with increased insulin sensitivity, reduced oxidative stress and modulation of the microbiota (Patterson et al., 2015).

Prolonged fasting – Fasting lasting longer than 48 hours, often 3 to 5 days, has been shown to reduce IGF-1 levels, increase autophagy and stimulate the regeneration of hematopoietic stem cells (Cheng et al., 2014). This type of fasting should be undertaken carefully and under supervision.

Dry fasting – This type does not allow either food or water. It can be absolute (no contact with water at all) or relative (showering is allowed, but drinking is not). Applied studies in Russia and Germany have reported noticeable anti-inflammatory effects and a rapid reduction in markers of oxidative stress (Wilhelmi de Toledo et al., 2019).

Fasting Mimicking Diet (FMD) – A method developed by Longo et al., which simulates fasting by calorie restriction (700–1100 kcal/day) for 5 days. Although food is present, the body responds as if in a fast, benefiting from protective and regenerative mechanisms (Brandhorst et al., 2015).

Traditional / spiritual fasting – Religious practices such as Ramadan or Orthodox fasting also have physiological effects. Studies show that religious fasting positively affects biological rhythms, metabolism and emotional state (Trepanowski & Bloomer, 2010).

Fasting, in all its forms, represents a natural biological strategy that helps the body balance metabolic activity, regenerate the immune system and stabilize the relationship with the microbiota. Thus, it is not merely a form of dietary control but an adaptive process suited for optimal organism function in different periods of modern life (Mattson et al., 2017).

Physiological phases of fasting

Fasting is not simply a cessation of food intake but a deep physiological process involving several dynamic phases of metabolic and hormonal reorganization. Over millions of years of evolution, the human body has developed efficient survival mechanisms, giving fasting a natural place within the body-mind-microbiota balance (Longo & Panda, 2016).

Below are the main phases that occur during fasting:

Phase one – Absorption and glucose utilization (0–12 hours): During this phase, the body continues to use glucose derived from the last meal. Insulin remains present in the circulation, maintaining signals for energy storage. Glucose is used primarily by the brain and central nervous system, as it is their main substrate. This phase remains postprandial and does not mark pronounced metabolic changes (Mattson et al., 2017).

Phase two – Transition to glycogenolysis and lipolysis (12–24 hours): When free glucose is depleted, the body moves to using glycogen stored in the liver. This reserve lasts approximately 12–24 hours and then, in the absence of glucose, the body activates lipolysis, breaking down fats into fatty acids and glycerol. Fatty acids are used by most cells for energy, while glycerol is converted into glucose for the brain via gluconeogenesis (Cahill, 2006).

Phase three – Ketogenesis and metabolic restructuring (after 24–72 hours): After glycogen stores are exhausted, the liver begins to produce ketone bodies which serve as an alternative energy source for the brain and muscles (Owen et al., 1967). This shift from using sugars to using fats and ketones is known as the 'metabolic switch' (Longo & Panda, 2016). The body enters a more efficient phase where it expends less and produces clean energy with less oxidative stress. This phase is accompanied by lower insulin levels, increased growth hormone and improved cellular sensitivity (de Cabo & Mattson, 2019).

Phase four – Activation of autophagy and cellular repair (48–72+ hours): In this phase autophagy deepens, which is the natural mechanism for clearing cells of debris, damaged proteins and dysfunctional organelles (Mizushima & Komatsu, 2011). It is like an internal cleaning process the body performs when not engaged in processing food. This process is essential for preventing degenerative diseases and maintaining longevity.

Phase five – Immune restructuring and cellular regeneration (after 3–5 days): Prolonged fasting promotes immune system regeneration, especially via hematopoietic stem cells. Valter Longo's laboratory studies have shown that the body begins to produce new immune cells after old, inflammatory and inefficient cells are eliminated (Cheng et al., 2014). This process is essential for people with weakened immunity or autoimmune diseases.

Refeeding – The most delicate phase: After fasting, the gradual reintroduction of food is as important as the fast itself. An inappropriate return with heavy fatty foods or sugar can lead to metabolic stress and severe fatigue. Therefore, a refeeding phase with light fruit, natural juices and light plant-based foods is recommended, maintaining clean foods to preserve the restructured microbiota and the benefits achieved (Wilhelmi de Toledo et al., 2019).

In conclusion, fasting follows a biological trajectory from the use of glucose reserves, through cellular cleansing, to immune regeneration. It is not merely abstaining from food but a natural biological journey of regulation, cleansing and renewal.

Mechanisms of metabolic change during fasting

Fasting is a powerful biological process that induces essential metabolic changes by activating survival mechanisms evolved to support organism function in the absence of food. These changes include the switch from glucose utilization to lipid and ketone utilization, hormonal modulation, cellular metabolic restructuring and the suppression of pro-inflammatory signals.

Switch from glycolysis to fatty acid oxidation: Under fasting conditions, the body depletes glucose and glycogen stores within 12–24 hours and switches to using fats as the primary energy source. Fatty acids are released through lipolysis and enter mitochondria where they are oxidized to produce ATP, the energy used by cells (Cahill, 2006). This shift from carbohydrate to fat utilization represents a profound metabolic change also known as the 'metabolic switch' (Longo & Panda, 2016).

Increased production of ketone bodies: The liver, during prolonged fasting, begins to synthesize ketone bodies (beta-hydroxybutyrate, acetoacetate), which are alternative energy sources for the brain, heart and muscles (Owen et al., 1967). Ketone bodies have neuroprotective roles, help reduce oxidative stress and have been shown to improve cognitive function and resistance to neurodegeneration (Newman & Verdin, 2014).

Lowered insulin and increased insulin sensitivity: One of the earliest effects of fasting is the reduction of insulin levels in the blood, which improves cellular insulin sensitivity. This is essential for preventing and treating insulin resistance and type 2 diabetes (Mattson et al., 2017). Fasting also lowers IGF-1 (Insulin-like Growth Factor 1), a hormone associated with aging and cancer (Fontana et al., 2010).

Activation of AMPK and inhibition of mTOR: Fasting increases AMPK (AMP-activated protein kinase) activity, an energy sensor that promotes fat utilization and inhibits lipid synthesis (Hardie et al., 2012). Simultaneously, fasting inhibits mTOR (mechanistic target of rapamycin), a protein complex that signals growth and cellular proliferation. mTOR inhibition is associated with increased longevity and cancer prevention (Madeo et al., 2019).

Activation of autophagy: One of the most important mechanisms of fasting is autophagy – a cellular cleaning and recycling process for damaged components inside the cell. This process is vital for maintaining cellular function and preventing neurodegenerative diseases, cancer and heart disease (Mizushima & Komatsu, 2011). Fasting naturally activates this mechanism in the absence of abundant amino acids and energy.

Modulation of inflammatory and oxidative responses: During fasting, inflammatory signals such as IL-6, TNF-α and CRP are reduced. Ketone bodies, especially beta-hydroxybutyrate, have an anti-inflammatory effect by inhibiting the activation of the NLRP3 inflammasome (Youm et al., 2015). Fasting also enhances antioxidant defenses by increasing the activity of enzymes such as SOD (superoxide dismutase) and glutathione peroxidase.

Stimulation of stem cells and cellular regeneration: In prolonged fasting, the organism shows the ability to activate stem cells, increasing the regenerative capacity of tissues. This has been observed in the immune system, where after a period of fasting there is elimination of old inflammatory cells and activation of new cells (Cheng et al., 2014). This process has implications for organ regeneration and health preservation in old age.

In conclusion, the mechanisms activated during fasting form a biological orchestra that guides the body toward cleansing, reorganization and regeneration. These processes explain many of the health benefits of fasting in metabolic, neurological and immune domains. Recent studies increasingly illuminate the complex biology underlying this ancient practice.

The role of fasting in mitochondrial health

Mitochondria – known as the cell's 'energy factories' – are essential components for maintaining metabolic, cellular and systemic balance. During fasting, mitochondria not only adapt to the lack of glucose supply but activate a range of protective and restorative mechanisms that improve their function and extend cellular longevity.

Activation of mitochondrial biogenesis: One of the most important effects of fasting is the stimulation of mitochondrial biogenesis – the process by which new mitochondria are created. This process is activated by factors such as PGC-1α (peroxisome proliferator-activated receptor gamma coactivator 1-alpha), which strengthens metabolic capacity during fasting.

Benefits of fasting for the organism

Fasting is an ancient biological mechanism that serves as an adaptation strategy in periods of food scarcity. Today, it has gained significant attention as a therapeutic tool for improving bodily functions, cellular regeneration and mental well-being. Its benefits are numerous and widely documented in the scientific literature.

Reduction of inflammation and oxidative stress

Fasting has demonstrated the ability to significantly reduce inflammatory biomarkers such as CRP, TNF-α and IL-6. These benefits result from reductions in glucose and insulin, which improve insulin sensitivity and decrease pro-inflammatory signaling (Longo & Panda, 2016). Simultaneously, fasting increases the activity of antioxidant enzymes such as superoxide dismutase (SOD) and catalase (Alirezaei et al., 2010), thereby reducing oxidative damage at the cellular level.

Microbiota as a barometer of fasting success

If fasting is performed in a controlled manner and is accompanied by a balanced diet, it promotes the re-emergence of beneficial microbiota populations in the gastrointestinal tract. The increase of short-chain fatty acid (SCFA)-producing bacteria is associated with improved metabolism, immunity and cognitive performance (Zhang et al., 2019).

Understanding self-cleansing crises (healing crises)

During fasting or strong dietary changes, the body may experience so-called 'self-cleansing crises'. These include headaches, extreme fatigue, fever, muscle pain and weakness due to the release of accumulated toxins (Buchinger & Wilhelmi de Toledo, 2020). In the absence of professional support, these symptoms are often interpreted as negative signals and lead people to interrupt fasting prematurely. In most cases, however, they are evidence of the body's reparative and mobilizing functions.

When a crisis turns into collapse: consequences of lack of guidance

If fasting is conducted in disorganized ways, without nutritional preparation and without medical supervision, many complications are at risk. Lack of balance during self-cleansing crises can lead to dehydration, metabolic burden, hypoglycemic crises and a marked reduction of the immune system. This condition is not a consequence of fasting itself, but of its mismanagement. In such situations, specialized advice and gradual refeeding are essential to prevent collapse.

Fasting and emotional detoxification

Fasting is not only abstaining from food for a certain period; it also requires emotional and psychosocial detoxification. By interrupting habitual ties to food, many people experience a range of emotions – from irritability and nervousness to increased concentration and calm. For many, this period is managed through psychological and traditional mechanisms (e.g., meditation, prayer) to cope with hunger and emotional concerns. When practiced mindfully and safely, fasting includes aspects of self-awareness and emotional release that help resolve disordered eating behaviors (Gearhardt et al., 2011; Goldhamer et al., 2021).

Fasting as a catalyst for mental cleansing

In religious and philosophical contexts, fasting has served as a tool for mental purification and increased awareness. After a period without food, the brain can enter a calmer and more focused state, partly due to elevated ketone body production (Newman & Verdin, 2014) and increased levels of BDNF (brain-derived neurotrophic factor). This mental clarity is also linked to reduced insulin spikes and lower brain inflammation (Longo & Panda, 2016). For many people, the fasting experience is perceived as a form of 'illumination' of the mind, a state of reflection and inner calm that contributes to overall well-being.

MATERIALS and METHODS

General aim of the study

This paper aims to analyze the impact of fasting on metabolism, the immune system and the microbiota, including concrete examples of biological mechanisms and laboratory changes documented during fasting.

Specific objectives

- To provide an expanded description of the impact of fasting on metabolic functions, the immune system and the microbiota.
- To highlight the biological mechanisms involved during fasting and the refeeding periods.
- To identify foods that favor the regeneration of the microbiota and the reduction of inflammation after fasting.
- To conduct laboratory analyses on several fresh foods and determine their composition in relation to support for the intestinal microbiota.
- To propose possible fasting protocols applicable and adapted to different health conditions.

Analysis of the scientific literature

A systematic review of the literature was conducted in international databases such as PubMed, ScienceDirect, Google Scholar and ResearchGate with the aim of summarizing the latest studies on fasting, the microbiota, metabolism and their interconnections. Keywords used included: fasting, microbiota, metabolism, remodeling, well-being, combined with supporting terms such as autophagy, SCFA, refeeding, gut-brain axis, stem cells, etc. Literature filtering was performed according to these criteria: articles in English, studies published primarily 2013–2023, studies from countries with scientific traditions and fasting practices and determination of links between fasting, microbiota and metabolism.

RESULTS and DISCUSSION

Results from the Literature

Recent research has emphasized the importance of the relationship between lifestyle, particularly fasting, and the composition of the intestinal microbiota. In particular, short-term and intermittent fasting protocols have been observed to cause noticeable changes in microbial diversity and in the ratio between beneficial and pathogenic species in the gastrointestinal tract (Zarrinpar et al., 2014).

An early study by Remely et al. (2015) showed that calorie restriction and fasting positively influence the Firmicutes/Bacteroidetes ratio, an important indicator of metabolic health and systemic inflammation. This shift toward a more balanced microbiome is associated with increases in bacteria such as Akkermansia muciniphila and Faecalibacterium prausnitzii, which are linked to improved intestinal barrier function and reduced endotoxemia (Cani et al., 2009).

Another important dimension in the literature is the impact of fasting on promoting neurogenesis and cognitive function, mediating the effect through ketone bodies and microbiota modulation (Mattson et al., 2018). Ketone bodies produced during fasting act as signaling molecules that stimulate neurotrophic factors such as BDNF (Brain-Derived Neurotrophic Factor), which influence mental clarity and resistance to oxidative stress.

The literature highlights that prolonged fasting (3–5 days) stimulates immune system regeneration via selective removal of damaged cells and an increase in hematopoietic stem cells (Cheng et al., 2014; Longo & Panda, 2016). This mechanism is linked to microbiota modulation and reduction of chronic intestinally-based inflammation.

Studies have also observed that food following a fasting period is critical for microbiota reconstruction. Diets rich in fiber, vegetables and fresh fruits favor colonization by beneficial bacteria and promote production of short-chain fatty acids (SCFAs) such as butyrate, which improves gut mucosal integrity (Koh et al., 2016).

Clinically, the microbiota of individuals who follow a lifestyle with regular fasting show reductions in inflammatory markers such as IL-6 and TNF-alpha compared with individuals on a typical Western diet (Wilhelmi de Toledo et al., 2019). Moreover, in animal models, fasting has been shown to help reduce the risk of neurodegenerative diseases such as Alzheimer's and Parkinson's through epigenetic mechanisms influenced by the microbiota (Singh et al., 2017).

Studies from different regions (e.g., Japan, France, USA, Germany) support the positive effects of fasting on microbial composition, but the impact varies depending on the baseline diet followed after fasting. In Albania, structured studies on this topic are lacking, underscoring the need for localized research related to typical dietary patterns and cultural traditions

Laboratory results and comparisons with the literature

This section presents the laboratory analyses carried out at the Laboratory of the Faculty of Biotechnology and Food (FBU), at the Food Research Center (QKU), grouped by the analyzed product categories and compared with literature data. Comparisons are illustrated with tables and interpretative comments, focusing on the impact of food components on the intestinal microbiota. Laboratory analyses confirm the role of fruits and vegetables as essential sources of components that nourish the microbiota, such as dietary fiber, antioxidants and beneficial fatty acids. These results align with recent studies emphasizing the importance of a diet rich in plant foods in shaping a diverse and stable microbiota (Conlon & Bird, 2014; Naliyadhara, et.al., 2023).

Table 1. Vitamin C content in fresh vegetables (mg/100g)

Product	Laboratory Result	Scientific Literature
Red Pepper	127	128
Yellow Pepper	110	120
Green Pepper	80	95
Tomato	25	23

Comment: Red and yellow peppers were found to be richer in vitamin C, consistent with the literature. The small differences are probably related to storage, exposure to light, or ripening of the product.

Table 2. Dietary fiber content (g/100g)

Product	Fiber (g/100g)
Avocado	6.7
Red Pepper	2.6
Yellow Pepper	2.4
Green Pepper	2.1
Tomato	1.2

Comment: Avocado is high in fiber, but its histamine load should also be considered. For sensitive individuals, substituting spinach or fresh peppers may be more appropriate. Fiber is important for the functioning of the microbiota. The table results serve to highlight the products that help the most in the growth of beneficial microbial colonies.

Comparing Arnold Ehret's Thoughts with Modern Approaches to Nutrition and the Microbiota

Arnold Ehret, in his work "The Mucusless Diet Healing System", emphasizes the importance of eliminating foods that create waste and mucus in the body, advocating a fruitarian diet and periods of fasting. He puts forward an idea that resonates strongly with modern studies on the microbiota and the impact of diet on digestive and metabolic health.

In this paper, Ehret's idea is taken as a comparative impetus to reflect on how a low-residue diet rich in soluble fiber (as found in fresh fruits and green vegetables) helps increase microbial diversity, reduce inflammation and improve well-being. This is compared with modern literature that emphasizes that a diet rich in complex carbohydrates, antioxidants and fiber promotes the development of a stable and healthy microbiota (Ehret, 2022).

CONCLUSION

- The intestinal microbiota, influenced by birth, feeding and lifestyle, represents an irreplaceable component of overall health.
- Fasting, as a natural physiological process, exhibits evident effects in remodeling the microbiota, favoring the increase of beneficial bacteria and the reduction of opportunistic and inflammatory ones.
- During fasting periods, adaptive cellular mechanisms are activated that increase insulin sensitivity, promote ketogenesis, reduce systemic inflammation and stimulate neurogenesis and circulation of neurotrophic factors.
- Multiple pieces of evidence from the literature suggest that intermittent fasting has potential as an adjunct strategy in the prevention and management of chronic diseases such as diabetes, obesity, mental disorders and neurodegenerative diseases.
- Laboratory results and comparisons with international literature indicate that the nutrient composition of fresh fruits and vegetables (without salt, without industrial processing) favors the maintenance of a healthy microbiota and the positive modulation of histamine.

Recommendations

- It is recommended at the institutional level (school, clinic, community) to promote awareness about the role of the microbiota and fasting in well-being.
- More scientific research should be encouraged on the effects of fasting on human microbiota, especially in Albanian and Mediterranean contexts.
- Fasting should be integrated into personalized nutritional programs, supervised by health professionals.
- The use of low-histamine-load diets and foods rich in prebiotic fibers should be promoted for individuals with intestinal sensitivity or metabolic disorders.
- Support should be given to the creation of pilot centers in Albania to apply and evaluate fasting and functional nutrition protocols in the rehabilitation of individuals with mild and chronic pathologies.

Additional Declaration

Author Contributions

The theoretical framework of the study was created by the first author, the data collection and analysis process was carried out by the the other authors, the article was written jointly by both authors and the final version was approved together. The contribution rates are first author (60%) and other authors (40%).

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Responsible Artificial Intelligence Statement

No artificial intelligence support was received in any part of this study.

Conflicts of Interest

The authors declare that there are no conflicts of interest related to the publication of this study.

Ethics Approval

In all processes of this study, the principles of Pen Academic Publishing Research Ethics Policy were followed.

This study does not require ethics committee approval as it does not involve any direct application on human or animal subjects.

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