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Exploring the Differential Impacts of Intermittent Fasting on Men and Women

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Abstract
Intermittent Fasting **(**IF) has recently become very popular due to its perceived health benefits, such as helping with weight loss, improving metabolic health, and even possibly influencing lifespan. This dietary strategy involves alternating between eating and not eating, with different fasting diets picking up popularity. Despite the fact that IF seems to improve general well-being, it is vital to look at the sex-specific outcomes because metabolism and hormonal profiles vary in men and women. This review focused on the biological pathways involved in IF, as well as the advantages and disadvantages associated with this procedure. In addition, it considers how IF specifically impacts male and female physiology in terms of hormonal shifts, metabolic modifications, energy reserves, metabolism, and aspects of fertility and reproduction. It is therefore imperative to characterise these sex differences with regard to IF strategies and maximise gender-sensitive benefits for males and females. However, we should conduct more studies to understand the complex effects of IF on individual sexual health and to identify individualised dietary patterns.
Keywords: *Intermittent fasting, Reproductive health, Sex-specific effects, Health benefits, Metabolic health, Longevity*

1. Introduction

There have been increasing discussions about the practice of Intermittent fasting (IF) as potentially effective and beneficial for improving human health and possibly increasing lifespan. Originating from the concepts of early civilisation and transforming into different forms of contemporary dieting, IF encompasses the cycles of feeding and starving (1). Scholars have viewed this approach as a tool for weight loss, enhancing metabolic rates, and mitigating age-related diseases. Despite the extensive literature on the beneficial effects and mechanisms of IF, it is now crucial to consider its impact in relation to gender differences (2). It is implicit that men and women have different metabolic, hormonal, and physiological profiles with regard to nutrient utilization and body responses to diets, leading to speculation about the specific effects of IF in males and females (3). This review seeks to provide a comprehensive analysis of the IF on the molecular level, its general importance for human health, possible adverse side effects, and differences in outcomes in males

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and females. Knowing how IF affects males and females differently will assist in fine-tuning dietary interventions and promoting the health of different groups.

2. Methodology

With this study, we reviewed existing data in the scientific literature that may illustrate the sex-specific impact of intermittent fasting. We conducted a thorough search using electronic sources such as PubMed, Google Scholar, and Scopus. The included keywords were intermittent fasting, sex-specific effects, hormonal regulation, body composition, fertility, and reproductive health. Peer-reviewed clinical articles, systematic reviews, and meta-analysis articles published in the last decade met the criteria for inclusion of the studies. The narrative synthesized data on the effects of intermittent fasting on hormonal changes, metabolic regulation, energy status, and particularly on the sexual functions of both males and females. We further analysed and summarised them to compare the differences and similarities between genders and intermittent fasting, providing a foundation for future research in the field and aiding in the development of individualised diet plans.

3. Overview of Intermittent Fasting (IF)

Nutrients are essential in the body, and a diet that contains them is important for a person's health and disease prevention (4,5). Fasting, or the deliberate avoidance of food and water, has a long history dating back to different religions and cultures. Since ancient times, people have practiced fasting as a spiritual or religious practice, or even as a health practice (6). For instance, Hippocrates, the father of medicine, encouraged fasting for health purposes in ancient Greece (7). Many religious cultures practice fasting, such as the Islamic month of Ramadan, the Christian practice of Lent, and the Jewish practice of Yom Kippur, which involves fasting as a means of purification, atonement, and discipline (8). From these precursors, contemporary fasting has evolved into a variety of fasting regimes for health and medicine. IF refers to meal timing that involves balancing between periods of eating and periods without food (9). In the early 21st century, IF surged mainly because published scientific research suggested that its application could help with weight loss, metabolic health, and even longevity (10). Intermittent fasting has evolved over time, with various types including Time-Restricted Feeding (TRF), Alternate-Day Fasting (ADF), Modified ADF, 5:2 Diet Whole Body Fat Loss, Eat Stop Eat, and Glimpse Meal Skipping. TRF entails 16 hours of fasting and 8 hours of eating, whereas ADF fasts for 24 hours and feasts for the remaining 24 hours. On fasting days, the modified ADF allows for up to 500 calories. The 5:2 diet reduces daily calorie intake to 500–600 calories, which is done on two separate days of the week (11,12).

4. Health Benefits of Intermittent Fasting

Many people have recently discussed intermittent fasting, as a technique to help achieve a healthy weight. This works by resulting in hormonal changes, better metabolic health, and better cholesterol levels (13). IF can also stimulate cellular repair and autophagy, increase life span, and increase gene expression (14). It can also reduce high blood pressure and inflammation while

enhancing brain function (15). It may also be effective in preventing neurodegenerative diseases, including Alzheimer's and Parkinson's diseases (16). It can extend a person's life, improve the digestive system, and potentially reduce the incidence of cancer (17). It may also improve cognitive functions such as memory and concentration, to name but a few; this may be due to steady glucose production and improved relaying of signals through neurotransmitters (18). IF can also prevent other noncommunicable diseases like diabetes mellitus type 2, and cardiovascular diseases (19). However, one must practice IF sustainably and always seek a physician's permission if one intends to practice fasting.

5. Risks and Potential Side Effects of Intermittent Fasting

IF is a valuable dietary technique that is known to have tremendous benefits, but like any other dietary regimen, it has potential drawbacks and adverse effects. These adverse effects include nutritional deficiencies, hunger and irritability, fatigue, disordered eating, impaired cognition, susceptibility to binge eating, gastrointestinal issues, negative effects on women's hormones, halitosis due to elevated blood and breath acetone levels, and muscle wasting (20,21). When planning for any fast, consultation with a healthcare provider is critical, especially if one has specific health issues or concerns about the practice (22).

6. Molecular Mechanisms Underlying Intermittent Fasting

Intermittent fasting (IF) has recently risen in popularity due to its general health, weight loss, metabolic, and aging benefits. The biological processes of intermittent fasting are intricate and diverse, and various molecular processes occur at the cellular and molecular level. Here are some key molecular mechanisms believed to be involved:

1. Metabolic Switch: It is a fact that during the periods of fasting, the body shifts to the use of fats for its energy needs instead of the glucose it gets from meals (23). These changes involve swap between oxidative and glycolytic metabolism, which is timed by changes in the blood insulin and glucagon concentrations (24). Insulin is the main hormone responsible for glucose metabolism (25,26). Insulin levels go down during fasting hence glucose uptake by the various cells is reduced while lipolysis or breakdown of fats for the release of fatty acids for use is enhanced (27).

2. Autophagy: Intermittent fasting also enhances autophagy, a process through which damaged or compromised cellular components are recycled. Autophagy contributes to the balance of cellular organelles, elimination of protein aggregates and also in restoration of damaged organelles (28). The process is controlled through nutrient signaling pathways, including mechanistic target of rapamycin (Mtor) and AMP-activated protein kinase (AMPK), respectively (29).

3. Hormonal Regulation: Intermittent fasting impacts different hormone levels present in an individual's body, such as insulin, glucagon, leptin, and ghrelin. These hormones are essential for metabolism management, as well as feelings of hunger and fullness (30). For example, effective fasting lowers insulin concentrations in the body, which aids in fat mobilization and increased ketones production (31). Also, fasting raises the levels of growth hormones that promote fat burning and help preserve muscles (32).

4. Gene Expression: Intermittent fasting has the ability to alter gene expression profiles that relate to cellular functions such as metabolism, inflammation, and stress (33). For instance, fasting increases the set of genes involved in mitochondrial generation, antioxidant protection, and DNA

repair (34). All these changes in gene expression lead to enhanced functional capacity and protect the cell from stress.
5. Inflammatory Pathways: Chronic inflammation is believed to be involved in the development of various diseases, such as obesity, type II diabetes, and heart disease (35,36). It is also suggested that IF reduces the level of pro-inflammatory cytokines and increases the level of anti-inflammatory molecules (37,38).
6. Oxidative Stress: Research suggests that intermittent fasting reduces oxidative stress by enhancing antioxidative protection and reducing the formation of reactive oxygen species (ROS) (39). Excessive production of ROS facilitates the emergence of some diseases like cancer, diabetes, and rheumatoid arthritis (40,41). Autophagy that results from fasting prompts the throwing out of damaged proteins and organelles, which has to do with the production of oxidative stress (42). Also, the ketone bodies formed during fasting have an anti-oxidative effect in the body by shielding the various human cells from free radicals (43).
7. Epigenetic Regulation: According to the available literature, there is some evidence that IF can impact epigenetic marks like DNA methylation and histone modifications, which control gene utilization even though the original genetic code in the DNA remains unaltered (44). These epigenetic changes may explain how intermittent fasting exerts its effects on metabolic health and longevity.

7. Sex-specific effects of intermittent fasting

There are some distinctions between male and female body metabolism and hormonal balance, which is why IF can have a different impact on the body. These are some of the sex-specific effects of intermittent fasting.
1. Hormonal Response: Fasting can alter hormone levels in the bodies of both male and female subjects, but in different ways. For instance, in males, rising levels of testosterone, growth hormone, and adrenaline that are a result of fasting may help boost fat metabolism and muscular development. Women's hormonal changes related to fasting may differ depending on the phase of the menstrual cycle and hormonal profile (45). Future research on the detrimental effects of intermittent fasting on reproductive hormones in women is necessary.
2. Body Composition Changes: Male and female subjects may have discrepancies in the changes in body composition with IF. Although both genders may experience similar weight loss and a decrease in body fat percentage during IF, the changes in fat distribution and muscle mass may be different. Men can have better improvement in the abdominal area, while women can benefit more from losing hip and thigh fat (46).
3. Energy Levels and Performance: During fasting periods, men and women may have different energy levels and performances. It is also believed that men can switch to fasting more easily and have higher energy levels, possibly due to metabolic or muscle differences; however, there are exceptions, and some women may also notice increased energy and better brain functioning during fasting (47).
4. Metabolic Adaptations: Research has suggested that the metabolic changes associated with IF may vary between men and women. For instance, men are likely to record better enhancements in metabolic characteristics like insulin sensitization and blood glucose levels than women because the latter are more sensitive to things like the phase of their menstrual cycle and hormonal balance

(48).

5. Fertility and Reproductive Health: Intermittent fasting is also associated with fertility and reproductive health, especially for women (49). Research has shown that severely restricting one's calorie intake or fasting for extended periods can negatively impact menstrual cycles and potentially affect fertility in women (50). Therefore, further research is necessary to determine the impact of intermittent fasting on sexual health among men and women.

8. Conclusion

IF is a beneficial concept for increasing the quality of life, for weight loss, for metabolism, and even for increasing the lifespan. However, the impact of IF is considered to be different in men and women, for example, in hormonal shifts, alterations in body composition, energy levels, and the reproductive system. To achieve this goal, it is critical to decipher these sex-specific effects in order to develop a proper dietary plan that can improve the health status of both sexes. While IF offers numerous benefits, it also reveals certain disadvantages that need careful consideration, particularly in relation to women's fertility. Additional studies are required to enhance the knowledge of these sex-related distinctions with a view to optimising IF approaches for sex-specific health promotion.

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