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PHYSIOLOGICAL ADAPTATIONS TO INTERMITTENT FASTING: ENDOCRINE AND METABOLIC RESPONSES

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Abstract

This review aims to explore the physiological adaptations resulting from intermittent fasting, and to understand the endocrine and metabolic responses. It also highlights the important role of intermittent fasting in modulating hormone secretion, improving metabolic efficiency, and promoting long-term overall health. The study was conducted using an analytical approach based on scientific studies on intermittent fasting and its effects on the body in particular and on health in general. The study focused on hormonal responses, including insulin, glucagon, cortisol, thyroid hormones, and growth hormone, along with key metabolic processes such as ketogenesis, autophagy, and mitochondrial adaptation. Review of previous research found that intermittent fasting lowers insulin levels and enhances glucagon secretion, supporting a metabolic shift toward fat oxidation. Short-term increases in cortisol are stabilized during fasting, and thyroid hormone metabolism regulates adaptive metabolism. Growth hormone levels rise during fasting, while insulin-like growth factor-1 levels decline, promoting autophagy. Intermittent fasting also enhances mitochondrial efficiency and reduces oxidative stress. The article proved that Intermittent fasting has profound physiological effects by recalibrating hormonal pathways and improving metabolic processes. These effects contribute to improved glucose control, lipid metabolism, and cellular plasticity. Clinical research supports the therapeutic potential of intermittent fasting in metabolic conditions, cardiovascular disease, and neurodegeneration. Further long-term clinical studies are recommended to confirm these findings.

Keyword: Intermittent fasting, Metabolic adaptation, Endocrine response, Hormonal regulation.

Introduction

Intermittent fasting (IF) is an eating pattern that involves alternating periods of fasting and eating. This pattern doesn't specify what foods to eat, but rather when to eat (De cabo,R.& Mattson,m. p. 2019) Abstaining from food (but not plain water) for a set period each day or week. Some common methods of intermittent fasting include: Alternating-day fasting. A person fasts completely on the first day or only eats a small meal (less than 500 calories), then eats a normal diet the next day, and so on(Varaday,K.A.(2011)). The 5:2 fast involves eating a normal diet five days a week and fasting for two days a week. Fasting involves specific times each day. The person eats normally

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but only during an 8-hour grace period each day. For example, the person skips breakfast but eats lunch at noon and dinner before 8 p. m. (Harvie, M. N., & Howell, A. (2017))

Physiologically, Intermittent fasting affects metabolic pathways and hormonal regulation by altering levels of certain hormones such as insulin, growth hormone, and glucocorticoids, in addition to modulating the immune response. Intermittent fasting can alter the metabolic immune response of cells and tissues, impacting metabolic flexibility and inflammation. This review research the new concepts of the endocrine and metabolic adaptations associated with IF, focus attention on its physiological and clinical implications. (De cabo,R.& Mattson,m.p.2019)

2. Theoretical Background of Intermittent Fasting

The physiological basis of fasting includes hormonal and metabolic changes in the body caused by abstaining from food. Fasting causes the body to use fat and ketone bodies as its primary source of energy instead of carbohydrates, which improves insulin sensitivity and helps regulate blood sugar levels(Cahill, G. F. (2006)). It also plays a major role in reduce oxidative stress, activating cellular repair mechanisms such as autophagy, a process that allows for the recycling of damaged organelles and large, aggregated, or malformed molecules These acclimation can improve hormonal cycles, energy expenditure, and metabolic health, serves as a basis for therapeutic applications of IF(Levine, B., & Kroemer, G. (2008)).

3. Endocrine Responses to Intermittent Fasting

Intermittent fasting (IF) has an impact on the endocrine system. It alters hormone secretion patterns, improves hormone sensitivity, and recalibrates circadian rhythms that influence key metabolic processes(Levine & Kroemer, 2008; de Cabo & Mattson, 2019). Among the most important hormonal changes associated with intermittent fasting are:

3.1 Insulin and Glucagon

Lower insulin levels and increased glucagon secretion are among the most prominent hormonal adaptations to intermittent fasting during fasting periods. Low glucose levels suppress insulin secretion and enhance glucagon activity, which converts stored glucose in the liver into a usable promotes form and promotes lipolysis p(hepatic gluconeogenesis)(Mattson et al., 2017). These changes support the metabolic shift from glucose to fat as the primary fuel source, thus improving insulin sensitivity over time (Patterson & Sears, 2017).

3.2 Cortisol and the HPA Axis Hypothalamic pituitary axis

A glucocorticoid hormone(Cortisol), orderly by the hypothalamic-pituitary-adrenal (HPA) axis, plays important role in glucose metabolism and responses of stress .(IF), causes a fleeting rise in cortisol levels, especially during early fasting stages, which helps load energy precautions through gluconeogenesis and proteolysis (Anton et al., 2018). Yet, in long-term intermittent fasting trials, cortisol levels tend to stabilize or decrease, possibly due to improved metabolic efficiency and regulation of circadian rhythms.

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3.3 Thyroid Hormones (T3 and T4)

Basal metabolic rate and thermogenesis regulate by thyroid hormones. Some research suggest that caloric privation for long time or fasting may lead to a decrease in triiodothyronine (T3) levels while maintaining normal levels of thyroxine (T4) and thyroid-stimulating hormone (TSH), refers to a protective metabolic adaptation more than pathological hypothyroidism (Muller et al., 2015). These changes may participate to increased metabolic competence and long life.

3.4 Growth Hormone (GH) and IGF-1

Growth hormone (GH) is strongly stimulated by fasting, thus supporting and aiding lipogenesis and maintaining lean body mass (Hu et al., 1988). Fasting often suppresses insulin-like growth factor-1 (IGF-1), which is associated with decreased anabolic signaling and cell proliferation (Longo and Panda, 2016). down regulation of IGF-1 may be attributed to increased autophagy and a decreased risk of cancer, especially during periods of periodic fasting (Brandhorst et al., 2015).

4. Metabolic Adaptations to Intermittent Fasting

The metabolic changes of intermittent fasting are extremely beneficial and health-promoting influence. These adaptations support energy efficiency, improve mitochondrial function, and shift substrate utilization toward fatty acid oxidation and ketone production. These processes enhance endurance, reduce oxidative damage, and prolong lifespan.

4.1 Ketogenesis and Fatty Acid Oxidation

During fasting the main energy source is ketone bodies which derived from fats as a major source of energy instead of glucose. when glycogen stores are consume, lipolysis increases, then releasing free fatty acids which converted to ketones bodies in the liver .Brain and muscle energy needs powered by ketogenesis. while reducing insulin levels and glucose dependence (Cahill, 2006).

4.2 Autophagy and Cellular Cleansing

Fasting strongly activate autophagy, it is a cellular degradation and recycling process, removes the organelles which damage , protein aggregates, and pathogens, cell renewal and homeostasis. This process helps to protects against neurodegeneration, inflammation, and cancer (Levine & Kroemer, 2008).

4.3 Mitochondrial Efficiency and Oxidative Stress

Free radicals or reactive oxygen species (ROS)are unstable molecules produced as a natural byproduct of cellular metabolism in the body. They can cause oxidative stress and damage cells, but fasting can help reduce their production or mitigate their effects .IF enhances the biogenesis and function of mitochondrial, leading to production ATP more efficient and less (ROS) generation. This contributes to improved metabolic flexibility and steadfastness against age-related decline
(Lopez-Lluch & Navas, 2016).

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5. Clinical Implications and Long-Term Outcomes of Intermittent Fasting

5.1 Obesity and Weight Management

IF certainly lead to body weight loos and decrease fat mass, particularly visceral fat, with preserving lean mass. fasting and adhering to specific eating times for an extended period of time improves satiety compared to standard calorie restriction. (Varady et al., 2013).

5.2 Type 2 Diabetes and Insulin Resistance

Sure IF improves insulin sensitivity and reduces fasting glucose and HbA1c levels in patients with prediabetes and type 2 diabetes. It may reduce medication dependency under clinical supervision (Sutton et al., 2018).

5.3 Cardiovascular Health

Intermittent fasting lowers blood pressure, LDL-C, triglycerides, and inflammatory markers like CRP, reducing cardiovascular risk (de Cabo & Mattson, 2019).

5.4 Neuroprotection and Cognitive Function

IF increases Brain –derived neurotropic factor (BDNF), enhances synaptic plasticity, and protects neurons from oxidative stress, offering potential protection against Alzheimer's and Parkinson's diseases (Mattson et al., 2018).

5.5 Cancer and Cell Proliferation

IF reduces insulin –like Growth Factor 1 (IGF-1), enhances autophagy, and protects normal cells during chemotherapy. Fasting-mimicking diets show promise in reducing tumor growth and recurrence (Brandhorst et al., 2015).

5.6 Risks and Contraindications

Individuals with certain conditions (e.g., pregnancy, eating disorders, adrenal insufficiency) may experience adverse effects from IF. Medical supervision is recommended in chronic illness cases (Harris et al., 2020).

6. Conclusion

Physiological adaptations that significantly influence both endocrine and metabolic systems through Intermittent fasting (IF). By modulating key hormonal pathways—such as insulin, glucagon, cortisol, thyroid hormones, and growth hormone—IF enhances hormonal sensitivity and promotes metabolic flexibility. These changes are accompanied by a shift toward fat utilization and ketone body production, increased mitochondrial efficiency, and the activation of cellular stress resistance me.

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