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Correlation Between Serum Ghrelin Levels and BMI in Both Obese and Non - Obese Individuals: A Review

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Abstract: ***This review article explores the relationship between serum ghrelin levels and Body Mass Index (BMI) in both obese and non - obese individuals. Ghrelin, a peptide hormone primarily secreted by the stomach, is known to regulate appetite and energy balance. Understanding the correlation between ghrelin levels and BMI can provide valuable insights into the mechanisms underlying obesity and metabolic regulation. Through a comprehensive analysis of existing literature, this review examines the current evidence regarding the association between ghrelin levels and BMI across diverse populations. The review discusses potential factors influencing this correlation, including dietary intake, meal timing, physical activity, and hormonal regulation. Additionally, the implications of variations in ghrelin levels for obesity management and potential therapeutic interventions are explored. Overall, this review aims to contribute to a deeper understanding of the complex interplay between ghrelin, BMI, and metabolic health in both obese and non - obese individuals.***

Keywords: Ghrelin, Body Mass Index (BMI), Obesity, Non – Obese

1. Introduction

Obesity can be defined as excess body fat, and it is believed to be linked to metabolic and endocrine issues with somatotropic release in physiological obesity. The stomach releases ghrelin, an acylated peptide hormone that acts as a mediator for the development of hormones secretory receptor. Ghrelin activation boosts growth hormone release and hunger, as well as glucose metabolism. In healthy persons, ghrelin levels rise during fasting and fall after meals. The prevalence of obesity has reached epidemic proportions globally, posing significant public health challenges. Obesity is associated with various metabolic complications, including insulin resistance, cardiovascular disease, and type 2 diabetes. Ghrelin, a peptide hormone predominantly produced in the stomach, has emerged as a key regulator of appetite and energy balance. Several studies have investigated the relationship between ghrelin levels and BMI, aiming to elucidate the mechanisms contributing to obesity and metabolic dysfunction. While some studies suggest a positive correlation between ghrelin levels and BMI, others report conflicting findings. Understanding the complexity of this relationship is essential for developing effective strategies for obesity prevention and management. This review aims to synthesize existing evidence on the correlation between serum ghrelin levels and BMI in both obese and non - obese individuals.

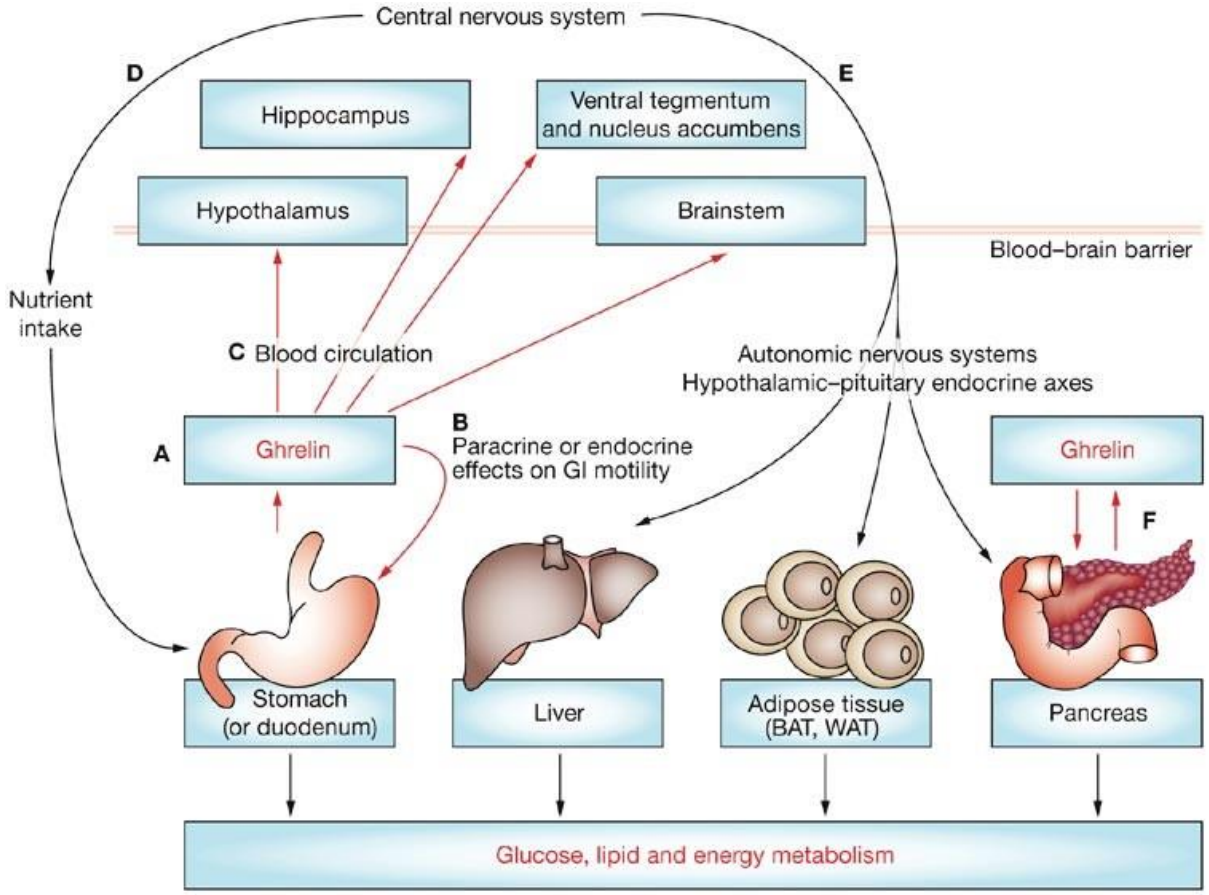

Figure 1: Relationship between Obesity and Ghrelin

2. Literature Review

The literature review systematically examines studies investigating the association between serum ghrelin levels and BMI in obese populations. Studies encompassing both cross - sectional and longitudinal designs are included to provide a comprehensive overview of the existing evidence. Factors such as age, gender, dietary habits, physical activity, and hormonal regulation are considered in the interpretation of findings. The review highlights the heterogeneity in study outcomes, with some studies reporting a positive correlation between ghrelin levels and BMI, while others find no significant association or even an inverse relationship. Potential explanations for these issues, including methodological differences, population characteristics, and confounding variables, are discussed. Furthermore, the review explores the role of ghrelin in appetite regulation, energy expenditure, and metabolic homeostasis, shedding light on its relevance for obesity pathophysiology.

Ghrelin is a hormone secreted by the stomach

The gene coding for human prepro - ghrelin, *GHRL*, is located on chromosome 3 and is composed of four exons and three introns spanning 5kb. Human prepro - ghrelin consists of 117 amino acids, and the mature ghrelin peptide is constituted of 28 amino acids with a fatty acid chain modification (octanoyl group) on the third amino acid. Ghrelin peptide was originally isolated from the stomach, but ghrelin protein has also been identified in other peripheral tissues, such as the gastrointestinal tract, pancreas, ovary and adrenal cortex. In the brain, ghrelin - producing neurones have been identified in the pituitary, in the hypothalamic ARC, and in a group of neurones adjacent to the third ventricle between the dorsal, ventral, paraventricular and arcuate hypothalamic nuclei.

Ghrelin binds to the growth hormone secretagogue receptor (GHS - R). By nucleotide sequence analysis Howard *et al*. identified two types of cDNA encoding for the GHS - R, which were derived from the same gene and were referred to as GHS - R1a and GHS - R1b. The gene encoding for the human GHS - R1 receptor is located on chromosome 3 and is constituted of two exons and one intron spanning 4kb. The GHS - R1a receptor is constituted of 366 amino acids. As to the GHS - R1b variant, it is not clear whether it is transcribed into protein *in vivo*, but theoretically it would code for 289 amino acids. The GHS - R1 receptor was originally cloned from the human pituitary and arcuate ventro - medial and infundibular hypothalamus.

The secretion of ghrelin by the stomach depends largely on the nutritional state. Ghrelin levels show pre - prandial increases and postprandial decreases. In addition, ghrelin levels show a diurnal variation and seem to be influenced by age, gender, BMI, growth hormone (GH), glucose and insulin. However, several of these correlations could not be confirmed. Notably, leptin has also been suggested to have influence on circulating ghrelin levels. It has been hypothesized that the satiety - inducing effects of leptin include the suppression of ghrelin secretion. Indeed, the effects of leptin on energy homeostasis are opposite (although not complementary) to those of ghrelin; leptin induces weight loss by suppression of food intake, whereas ghrelin functions as an appetite - stimulatory signal. Moreover, leptin has been shown to be an upstream regulator of ghrelin in rodents.

However, several studies in humans have produced conflicting results. For example, Tschop *et al*. demonstrated that in obese patients fasting plasma ghrelin levels are negatively correlated with fasting plasma leptin levels. However, in another study fasting plasma leptin and ghrelin concentrations were not correlated in obese children and adolescents. In addition, inter meal ghrelin levels are displaying a diurnal rhythm that is in phase with that of leptin in healthy humans. Furthermore, a recent study showed that leptin administration to healthy volunteers does not regulate ghrelin levels over several hours to a few days. These results suggest that leptin does not regulate circulating ghrelin levels. It is therefore possible that the leptin and ghrelin systems function independently of each other in the control of energy homeostasis.

The role of ghrelin in food intake is mediated through the hypothalamus

The effects of ghrelin on energy balance are at least in a large part mediated by the hypothalamus. Korbonits *et al*. proposed three different pathways for the appetite - inducing effects of ghrelin. First, after release into the bloodstream by the stomach, ghrelin may cross the BBB and bind to its receptors in the hypothalamus. Second, ghrelin may reach the brain through the vagal nerve and nucleus tractus solitarus. Third, ghrelin is produced locally in the hypothalamus, where it may directly affect the various hypothalamic nuclei.

Ghrelin attenuates leptin - induced reduction in food intake and body weight by modulating the expression of various hypothalamic peptides. Ghrelin stimulates the activity of neurones expressing NPY, AgRP and orexin. On the other hand, ghrelin has an inhibitory effect on POMC neurones and CRH - producing neurones. Ghrelin does not seem to be a direct regulator of leptin, as fasting produces identical decreases in serum leptin in ghrelin null and wild - type mice. The results gathered so far indicate that leptin and ghrelin have different effects on the hypothalamic neurones producing the various orexigenic and anorexigenic peptides, resulting in more or less opposing effects on energy balance.

3. Discussion

The discussion section synthesizes the key findings from the literature review and offers insights into the underlying mechanisms linking ghrelin levels and BMI. Possible explanations for the observed variations in ghrelin - BMI correlation across studies are critically evaluated, taking into account the complexity of metabolic regulation. The influence of dietary factors, such as macronutrient composition and meal timing, on ghrelin secretion and subsequent appetite modulation is discussed. Moreover, the potential impact of lifestyle interventions, including dietary modifications and physical activity, on ghrelin levels and BMI is examined. The discussion also addresses the implications of ghrelin dysregulation for obesity management and the development of pharmacological interventions targeting ghrelin signalling pathways.

4. Conclusion

In conclusion, this review highlights the complex interplay between serum ghrelin levels and BMI in both obese and non - obese individuals. While the evidence regarding the correlation between ghrelin levels and BMI remains inconclusive, a nuanced understanding of this relationship is crucial for elucidating the pathophysiology of obesity and metabolic disorders. Future research efforts should aim to address the methodological limitations of existing studies and explore potential mediators of the ghrelin - BMI association.

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