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Eating Disorder Biomarkers: Macronutrient Regulation of Ghrelin and Leptin

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Abstract:
This review examines the potential of ghrelin and leptin as biomarkers in eating disorders by analysing their roles in appetite regulation, energy balance, and eating behaviour. Ghrelin stimulates hunger, whereas leptin suppresses appetite and maintains energy homeostasis. Dysregulation of these hormones, often influenced by high-fat and high-sugar diets, is linked to overeating, obesity, and eating disorders. Imbalances in ghrelin and leptin signalling are associated with conditions such as hyperphagia and binge eating. This review also explores effects of stress and hormonal resistance on these hormones. Understanding how ghrelin and leptin interact with central and peripheral systems offers insights into appetite regulation and potential therapeutic targets for metabolic and psychological disorders.

Keywords: Ghrelin; Leptin; Eating disorders; Biomarkers; Biochemical.

1. INTRODUCTION

Ghrelin and leptin are two critical hormones that play opposing roles in the regulation of hunger, appetite, and energy balance. Ghrelin acts as a potent stimulator of appetite and food intake, particularly during fasting conditions. In contrast, leptin functions to signal satiety and regulate energy expenditure. These hormones not only maintain energy homeostasis but also influence complex physiological processes such as growth, metabolism, mood regulation, and reward-driven eating behaviours.

Recent research highlights the complex interplay between ghrelin and leptin in response to dietary macronutrients and palatable foods, with significant implications for understanding eating behaviours, obesity, and related metabolic disorders. The secretion and activity of ghrelin and leptin are tightly regulated by macronutrient composition, meal timing, and overall energy status. Ghrelin levels typically rise before meals and decrease postprandially, particularly in response to carbohydrate- and protein-rich meals. Conversely, leptin secretion is primarily influenced by adipose tissue stores and is modulated by chronic dietary patterns rather than acute nutrient intake. The dynamic interaction between these hormones is further complicated by the hedonic aspects of food consumption, where highly palatable, energy-dense foods can override normal homeostatic signals, leading to dysregulated appetite control and increased susceptibility to eating disorders.

Furthermore, ghrelin and leptin exert significant effects on the central nervous system, particularly in brain regions associated with reward, motivation, and emotional regulation. Ghrelin enhances dopaminergic activity in the mesolimbic pathway, reinforcing food-seeking behavior, while leptin dampens these reward responses to prevent excessive intake. Alterations in these neurohormonal pathways are implicated in various eating disorders, including anorexia nervosa, bulimia nervosa, and binge-eating disorder. Understanding the neurobiological mechanisms by which these hormones influence reward processing and emotional eating may offer new therapeutic strategies for managing pathological eating behaviors.

Given their complex involvement in both metabolic and psychological processes, ghrelin and leptin have garnered attention as potential biomarkers for diagnosing and monitoring eating disorders. Dysregulation of these hormones is often observed in individuals with obesity, restrictive eating disorders, and other abnormal feeding behaviors. By elucidating the effects of different macronutrient compositions on ghrelin and leptin dynamics, future research may provide targeted dietary interventions and pharmacological approaches aimed at restoring hormonal balance and

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improving clinical outcomes in affected individuals. Therefore, this review aims to explore the broader physiological and psychological influences of these hormones and their potential as biomarkers and therapeutic targets for managing eating disorders and food-related abnormal behaviours.

2. GHRELIN

Ghrelin hormone is primarily recognized as a gut hormone that stimulates hunger and initiate food intake, and regulates hedonistic eating and reward-driven eating behaviour during stress (1). Ghrelin was first discovered by Kojima and Kangawa (2) as a stimulator of growth hormone (GH) secretion, ghrelin is a 28-amino acid peptide with an n-octanoyl modification at the third serine residue (Ser-3). This potent hormone is primarily released by X/A-like cells in the oxyntic mucosa of the stomach (3). Ghrelin acts both centrally and peripherally systems, circulating in the bloodstream primarily during fasting conditions. It induces hunger, regulates appetite and energy balance, and stimulates food intake (4). Additionally, ghrelin plays a significant role in the regulation of growth hormone plasma levels, promoting weight gain, increasing lean muscle mass, and mitigating adipose tissue loss (5, 6).

GHRL, the ghrelin gene, produces a precursor peptide known as preproghrelin, consisting of 117 amino acids (7) (Figure 1). Preproghrelin undergoes post-translational processing to yield proghrelin, which is acylated by *ghrelin O-acyltransferase (GOAT)* at Ser3 with an octanoic acid group in the endoplasmic reticulum, forming acyl-ghrelin (active form) (8). Des-acyl ghrelin (inactive form) is generated from acyl-ghrelin by the removal of the octanoic acid group, typically after secretion. Acyl-ghrelin constitutes approximately 10% of total ghrelin (9). Previously it is suggested that only acyl-ghrelin has biological significant functions (10). However, recent studies have shown that des-acyl ghrelin could influence glucose metabolism, cell proliferation, and cardiovascular health despite it does not bind to the ghrelin receptor (*GHS-R1a*) as acyl ghrelin (11).

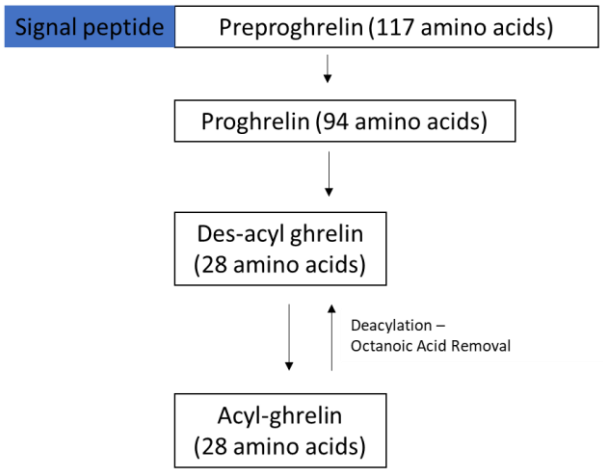

Figure 1. Processing of ghrelin.

Ghrelin exerts its effects by binding to the growth hormone secretagogue receptor (GHSR), a seven-transmembrane G protein-coupled receptor with two subtypes: GHSR1a (active) and GHSR1b (modulatory) (12). As summarized in Figure 2, GHSR1a is the functional receptor that is highly expressed in regions of the central nervous system (CNS), including the hypothalamus, ventral tegmental area (VTA), amygdala, and hippocampus (13). It is activated by acyl-ghrelin, triggering intracellular signalling cascades that lead to the release of growth hormone, thereby regulating growth, metabolism, and body composition (3). Additionally, GHSR1a activation in the VTA plays a critical role in regulating motivated behaviours (14). In contrast, GHSR1b is a splice variant and the dominant-negative form of GHSR1a, which it does not bind ghrelin or initiate direct signalling. Instead, it modulates GHSR1a activity through heterodimerization (14, 15). Although the exact function of GHSR1b remains unclear, it is believed to influence GHSR1a signalling and is expressed in the pituitary gland and pancreatic islets, where it may play a role in growth hormone secretion and insulin release (3, 15). Beyond the CNS, GHSR is widely expressed in peripheral tissues, including the pituitary, pancreatic islets, adrenal glands, thyroid gland, myocardium, and various brainstem nuclei such as the hippocampus, substantia nigra pars compacta (SNpc), VTA, and raphe nuclei (11). This widespread expression highlights the broader physiological roles of ghrelin in endocrine function, metabolism, and energy homeostasis.

The vast distribution of *GHSR1a* gives ghrelin the ability to affect a wide range of brain functions, including learning, memory, motivation, stress responses, anxiety, and mood regulation. It plays a significant role in regulating the hypothalamic-pituitary-adrenal (HPA) axis, influencing anxiety and mood disorders such as depression and fear (16). Ghrelin's influence on the motivation and reward system has also been linked to novelty-seeking behaviours. For instance, an in vivo study using male rats administered with ghrelin displayed a stronger preference for novel environments and greater exploration of new objects (17). Hence, it has gained considerable attention as a potential biomarker for eating disorders and food-related abnormal behaviours in both humans and animals (1, 18).

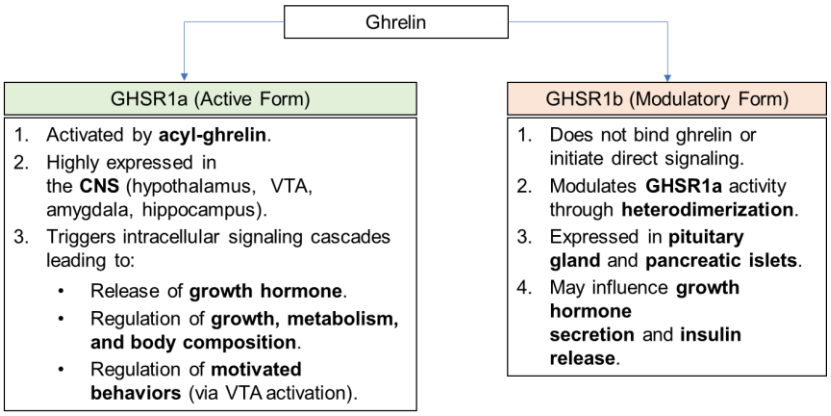

Figure 2. Summary of ghrelin and its receptor interaction.

3. LEPTIN

Since its discovery by Jeffrey M. Friedman's research team at Rockefeller University in 1994, leptin has been extensively studied for its critical role as a regulator of energy balance, primarily through its actions on the hypothalamus (19). Also known as the satiety hormone, leptin is a 167-residue peptide hormone with a 21-amino acid N-terminal secretory-signal sequence synthesized by the *Lep* gene (20). Leptin primarily functions to regulate satiety, body weight, and energy expenditure (19). The hormone is secreted mainly by adipocytes; thus, its concentration in the bloodstream is directly correlated with the body's fat reserves (21). Hence, leptin was initially recognized for its role in protecting against obesity, as demonstrated by the severe obesity observed in leptin-deficient *ob/ob mice*, which sparked considerable interest in its metabolic functions (22). Leptin is also produced in other tissues, including brain nuclei (23), bone marrow (24), ovaries (25), placenta (26), and stomach (27), suggesting that leptin has diverse physiological roles beyond regulating energy balance.

After secreted by adipose tissue, leptin enters the bloodstream and reaches its target tissues through several mechanisms (28) (Figure 3). It crosses into the brain through circumventricular organs, via saturable transport across the blood-brain barrier, and uptake into the brain parenchyma and choroid plexus (22). Once in the brain, leptin binds to its receptor, LepR, which exists in several isoforms due to alternative splicing (28). The longest form, *LepRb*, serves as the primary mediator of leptin's physiological effects (29). Upon binding to *LepRb*, leptin activates multiple downstream signalling pathways, including the Janus kinase 2 (*JAK2*)/signal transducer and activator of transcription (*STAT3*), *STAT*5, extracellular-signal-regulated kinase (*ERK*), and phosphoinositide-3 kinase (*PI3K*) pathways (30). Leptin-mediated activation of the *STAT3* pathway induces feedback inhibition through the increased expression of suppressors of cytokine signalling 3 (*SOCS3*) and protein tyrosine phosphatase 1B (*PTP1B*), which leads to a reduction in leptin sensitivity (31). Shorter forms of *LepR* lack the intracellular domains required for signal transduction and are mainly involved in leptin transport and degradation (21). Therefore, while these shorter isoforms contribute to maintaining leptin levels, their functional activity is considered minimal compared to *LepRb* (28).

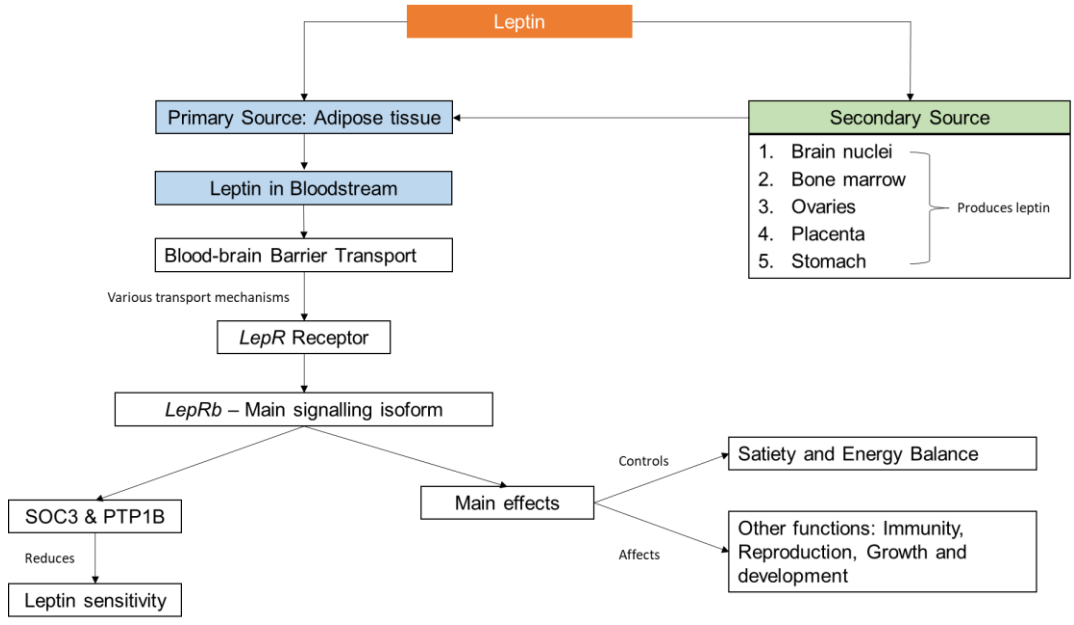

Figure 3. Leptin signalling system and its physiological implications.

Similar to ghrelin, leptin influences satiety by acting on the ventromedial hypothalamus (32). Leptin antagonizes the effects of ghrelin by inhibiting the lateral hypothalamus, thereby diminishing the stimulation of hunger (28). Leptin also communicates signals to the medial hypothalamus to regulate the body's energy storage (33). Maintaining appropriate levels of functional leptin is critical for numerous physiological functions, including reproduction, tissue remodelling, growth and development, and immune system regulation (9). A review by Kim *et al.* (34) highlighted that elevated circulating leptin levels inhibit food intake and increase energy expenditure under normal physiological conditions. Conversely, lower leptin levels stimulate increased food intake, reduce energy expenditure, and promote energy storage. Due to its action on the dopaminergic reward system, dysregulation of leptin is postulated to be one of the factors contributing to the psychopathology of eating disorders in humans.

4. INFLUENCE OF DIETARY MACRONUTRIENTS AND PALATABLE FOOD ON GHRELIN AND LEPTIN

As illustrated in Figure 4, ghrelin levels typically rise before meals (pre-prandial), sending hunger signals to the hypothalamus to stimulate appetite and initiate food intake (35). Ghrelin levels reduce postprandially because of the distension of the stomach by food sends inhibitory signals via the vagus nerve to the brain and stomach, suppressing ghrelin secretion (36). The production of ghrelin is also regulated by insulin, cholecystokinin (CCK), and glucagon-like peptide-1 (GLP-1), which are released during the digestion and absorption of macronutrients in the stomach and small intestine (37). In contrast, leptin levels are low pre-prandially and rise post-prandially, with leptin being released in response to food intake (19). As the stomach stretches during food consumption, vagal nerve signals are activated, which primarily influence the release of gut peptides like cholecystokinin (CCK) and peptide YY (PYY) that promote satiety (38). Leptin, which is released from adipocytes, primarily responds to changes in energy balance and fat storage, not directly to stomach stretching (39). Additionally, elevated insulin levels, which occur after the absorption of nutrients, enhance leptin production (40). These signals contribute to the suppression of hunger and reduce the production of ghrelin (Figure 4).

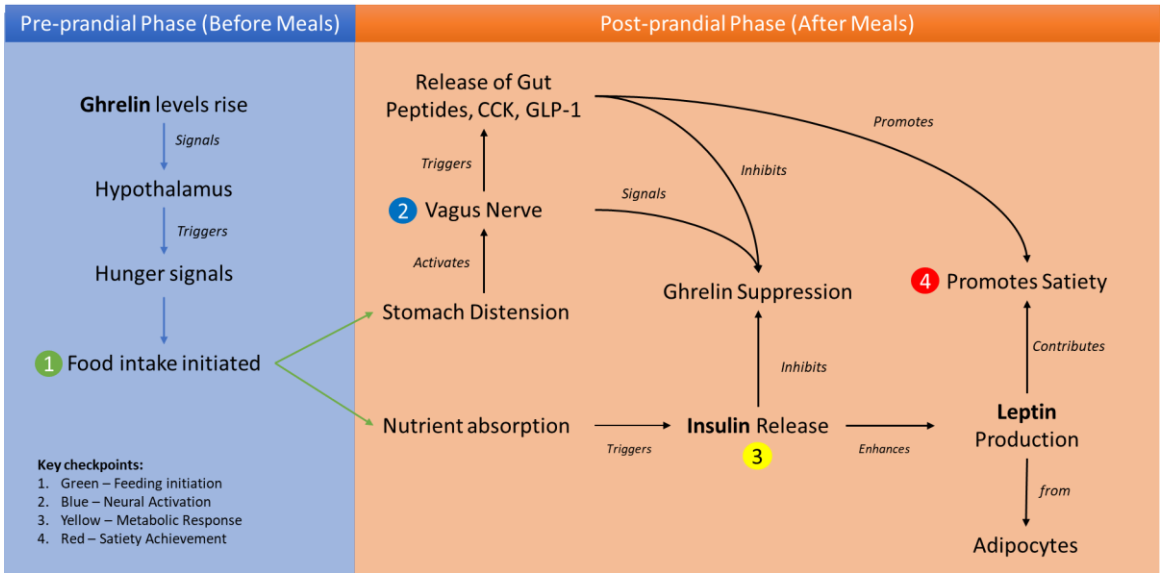

Figure 4. Mechanism of ghrelin and leptin regulation in appetite control.

The levels of leptin and ghrelin are closely associated with macronutrient dietary intake. For instance, Koliaki *et al.* (41) found that carbohydrates are the most effective at suppressing ghrelin levels due to their rapid absorption and stimulation of insulin secretion, while protein provides sustained ghrelin suppression, making it the most satiating macronutrient. Similarly, in a food-choice in vivo experiment, rats with a preference for fat exhibited lower plasma ghrelin levels compared to those favouring carbohydrates, suggesting that ghrelin secretion is highly sensitive to dietary composition (23). Furthermore, protein enhances satiety more effectively than other macronutrients, with higher protein intake being linked to increased leptin levels, contributing to reduced appetite and improved weight management (42). Additionally, Mendoza-Herrera *et al.* (43) discuss in their review that leptin levels only respond to specific types of dietary fat, such as alpha-linolenic acid (Omega-3), while they remain unaffected by monounsaturated and omega-6 polyunsaturated fatty acids. Whereas Mazza *et al.* (44) discussed that a high-protein diet, when combined with a stable carbohydrate intake, led to reduced calorie consumption. This effect is likely due to increased leptin sensitivity in the central nervous system, contributing to better appetite regulation.

Palatable foods are those that are pleasant to taste, while hyper-palatable diets are those containing specific combinations of ingredients (such as high fat, protein, or carbohydrates) that trigger reward centres in the brain, promoting overconsumption (8). While macronutrients influence ghrelin and leptin levels, the consumption of palatable foods is modulated by these hormones through their regulation of hunger, satiety, and reward pathways in the brain (45). GHSR1a plays a key role in driving the consumption of palatable foods, primarily by responding to the ghrelin hormone, which stimulates food intake beyond the body's metabolic needs (15, 46). For instance, the direct administration of

ghrelin into the mesolimbic reward nodes, specifically the VTA and nucleus accumbens (NAcc), resulted in a significant increase in feeding behaviour (47). Administration of ghrelin to the VTA in rats also increased their preference for environments associated with high-fat diets and enhanced operant responding for high-fat diet rewards, further suggesting its role in promoting food-directed behaviours (14).

Ghrelin also enhances the desire for sweet-tasting food, regardless of calorie content, suggesting that it may drive reward-seeking behaviours related to food (48). Nevertheless, Lockie *et al.* (49) demonstrated that diet-induced obesity (DIO) leads to ghrelin resistance, impairing reward processing pathways. While the ventral tegmental area (VTA) is central to reward signalling, the study suggests that ghrelin resistance may arise from upstream pathways rather than directly within the VTA. Furthermore, both ghrelin knockout (KO) and DIO mice showed reduced consumption of sweet substances like sucrose and saccharin, indicating anhedonia and highlighting the critical role of ghrelin signalling in mediating the pleasure derived from sweet-tasting foods.

Conversely, leptin modulates non-homeostatic eating behaviour by diminishing the rewarding aspects of food, thereby reducing the food intake and cravings for palatable items (20). Individuals with congenital leptin deficiency demonstrate heightened preferences for food and exhibit hyperphagia which were alleviated with leptin replacement therapy (50). Further study in mice show that leptin decreases the reward value of sucrose by reducing dopaminergic neuron signalling, underscoring its role in reward regulation (51, 52). Another study in mice similarly found that leptin diminishes food reward-seeking behaviours by acting on the dopamine system (53).

While current research provides valuable insights into the roles of ghrelin and leptin in regulating hunger, satiety, and reward-driven eating behaviours, several gaps in knowledge remain. Most studies focus on the acute impacts of individual macronutrients or specific dietary patterns on these hormones, with limited exploration of long-term hormonal adaptations to chronic dietary habits or hyper-palatable diets. Additionally, while the influence of ghrelin and leptin on reward pathways is well-documented, the mechanisms through which ghrelin resistance and leptin sensitivity modulate eating behaviours in the context of obesity and metabolic diseases require further investigation. The interplay between ghrelin and leptin in co-regulating hedonic and homeostatic pathways, particularly under different physiological or pathological states, is not fully understood. Addressing these gaps will provide a more comprehensive view of how these hormones influence eating behaviours and may inform novel interventions for obesity and eating disorders.

5. GHRELIN AS BIOMARKERS FOR EATING DISORDERS

Ghrelin has been extensively studied in patients with eating disorders due to its significant role in the reward system associated with eating. The hormone influences the brain's processes that govern learned feeding behaviours, which are shaped by external cues (such as the sight of food) and internal signals (like hunger), both of which significantly affect food consumption (54). Previous studies found there were significant discrepancy in ghrelin and leptin levels among eating disorder patients. For instance, a comparison study between 55 severely obese and 29 normal weight women by (55) found obese women exhibited lower fasting plasma acyl-ghrelin levels compared to normal-weight women. However, some obese women had unexpectedly high fasting acyl-ghrelin levels, approaching those of normal-weight participants, and scored higher on Drive for Thinness, suggesting a potential role for ghrelin as a biomarker for eating disorder vulnerability among obese women.

Interestingly, a cross-sectional study by Perna *et al*. (56) identified a possible interaction between deacyl-ghrelin and binge eating. Additionally, a systematic review and meta-analysis found that individuals with anorexia nervosa, both in restricting and binge-eating/purging subtypes, have elevated levels of both acyl- and deacyl-ghrelin (57). This analysis showed that increased blood levels of ghrelin were consistent across both subtypes of the disorder, suggesting a potential role of ghrelin in the pathophysiology of anorexia nervosa, including its influence on hunger and food intake regulation.

Kim *et al*. (34) also found that baseline ghrelin levels were associated with future weight gain in individuals with anorexia nervosa. Specifically, higher baseline ghrelin levels predicted prospective weight gain suggesting that elevated ghrelin may play a role in weight recovery in anorexia nervosa. In another study, ghrelin injections into the VTA of fasting rats on a high-fat diet resulted in increased food intake and weight gain in a dose-dependent manner. This suggests that ghrelin signalling in the VTA plays a role in both reward-based eating and fasting-induced hyperphagia, particularly with high-fat foods. If not regulated, this mechanism may contribute to overeating behaviours, including binge-like eating patterns.

Similar trends were also observed in animal studies; for instance, ghrelin levels were associated with feeding-related abnormal behaviours in horses caused by high-starch diets (58). Intervention with a high-fibre diet ameliorated the occurrence of these behaviours, as well as endogenous ghrelin levels, and simultaneously increased leptin levels (59). Similar findings were also observed in a previous study on pregnant sows fed a high-fibre diet, which demonstrated reduced oral stereotypic behaviours and lower ghrelin levels, likely due to increased satiety and reduced hunger-related behaviours (60).

Moreover, recent studies suggest that ghrelin may serve as a potential biomarker for food-related stress (61). Yamada (13) highlighted that ghrelin levels fluctuate in response to stress, with abnormal ghrelin dynamics linked to appetite disturbances in various psychological states, with notable differences observed based on sex and age. For instance, ghrelin levels were elevated after acute stress interventions, with obese individuals showing prolonged increases compared to non-obese individuals (1). Long-term alterations in ghrelin levels have also been found in patients with childhood trauma, potentially contributing to overeating behaviours in individuals with binge-eating disorder (62). A study by Brockway *et al*. (63) demonstrated that ghrelin administration directly into the arcuate nucleus (ArcN) and paraventricular nucleus (PVN) of the hypothalamus in Sprague-Dawley rats increased anxiety-like behaviours, particularly when food was not available post-injection. This suggests that ghrelin plays a significant role in stress

regulation, especially under conditions of food scarcity. These findings underscore the need for further investigation into ghrelin as a target for therapeutic interventions in eating disorders.

6. LEPTIN AS BIOMARKERS FOR EATING DISORDERS

Due to its synergistic relationship with ghrelin, incorporating leptin into ghrelin studies on eating disorders or food-related abnormal behaviours could provide a deeper understanding of the complex mechanisms underlying these disorders. Several studies have shown that patients with obesity, anorexia nervosa, bulimia nervosa, and binge eating disorder exhibit dysregulation in leptin levels. Despite its primary role in inducing satiety, individuals with obesity, particularly those with hyperphagic (excessive) eating habits as well as binge eating disorder often exhibit lower leptin levels compared to healthy individuals. In contrast, anorexia or bulimia nervosa patients tend to have higher leptin levels than healthy individuals.

Obesity is frequently associated with leptin resistance, a condition in which the brain becomes less responsive to leptin due to prolonged exposure to high leptin levels (28, 64). Leptin resistance is characterized by reduced receptor sensitivity in the central nervous system and disruptions in signalling pathways, such as STAT3, due to inhibitors like SOCS3 and PTP1B (21). This reduced sensitivity impairs the brain's ability to regulate appetite and energy expenditure, leading to difficulties in suppressing hunger and challenges in maintaining energy balance (65, 66). A study by Asai *et al.* (67) demonstrated that mice with reduced leptin production exhibited spontaneous overeating and significant weight gain. Similarly, Obradovic *et al*. (28) and Pena-Leon *et al*. (68) reported that high circulating leptin levels failed to inhibit hunger in obese patients. Moreover, leptin resistance is also closely associated with several metabolic disturbances, including insulin resistance, hyperinsulinemia, and an increased risk of cardiovascular diseases. These conditions can trigger chronic subclinical inflammation, further exacerbating metabolic syndrome and related disorders (69-71).

Binge eating disorder (BED) is characterized by recurrent episodes of excessive food intake, accompanied by a loss of control overeating (72). Episodes of binge eating are driven by stress-induced hormonal dysregulation, including decreased ghrelin and increased leptin levels, which impair hunger and satiety signals. This hormonal imbalance, coupled with altered dopamine activity in reward-related brain regions such as the nucleus accumbens and prefrontal cortex, reinforces compulsive eating behaviours (73). Compared to other eating disorders and healthy controls, patients with BED exhibit significantly higher leptin levels, even after accounting for BMI, indicating that leptin variations in BED are not solely dependent on weight (74). Elevated leptin levels in BED patients have been observed to impair food-specific inhibitory control, further reinforcing compulsive eating behaviours, a hallmark of BED (74, 75). In a rat model with intermittent access to palatable diets, leptin was found to modulate food-seeking behaviours by acting on neural circuits, with leptin-sensitive neurons in the anterior insula showing decreased excitability. This highlights an extrahypothalamic role for leptin in regulating food reward (76). The authors suggest that leptin dysregulation not only affects hunger and satiety but also influences higher-order decision-making processes, further reinforcing the compulsive eating behaviours characteristic of BED.

Conversely, leptin levels are significantly reduced in anorexia nervosa (AN) patients due to fat store depletion from severe undernutrition, a condition known as hypoleptinemia (77, 78). A longitudinal study by Stroe-Kunold *et al.* (79) observed low leptin levels in AN patient, which later increased significantly during inpatient treatment as their BMI improved. A significant characteristic of AN is altered energy balance and impaired neuroendocrine function due to low leptin levels that disrupt the JAK-STAT signalling pathway in the hypothalamus, particularly in the arcuate, dorsomedial, ventromedial, and paraventricular nuclei (80, 81). In addition to hypothalamic dysregulation, hypoleptinemia in AN profoundly impacts the neuroendocrine axes, including the hypothalamic-pituitary-thyroid (HPT) and hypothalamic-pituitary-gonadal (HPG) axes, which may lead to amenorrhea and hyperactivity. These alterations reflect the body's adaptive response to prolonged starvation, aimed at energy conservation (82, 83).

Studies on Bulimia Nervosa (BN) are challenging, with inconsistent findings regarding leptin levels, as some studies indicate altered levels (80). Cassioli *et al*. (74) highlighted a negative correlation between leptin levels and behaviours like binge eating and purging in BN, suggesting that lower leptin levels are associated with an increased frequency of these behaviours. Additionally, alterations in leptin signalling have been shown to influence eating behaviour aberrations in BN patients by affecting dopamine pathways linked to reward processing (84). Recent findings from Targa *et al*. (85) accentuate the significance of leptin-induced modifications in the JAK2/STAT3 pathway within the hippocampus, highlighting on how leptin influences synaptic plasticity and behaviour that facilitate pathophysiology of BN.

These studies underscore the critical role of leptin in regulating hunger, satiety, and higher-order decision-making processes, with its dysregulation contributing to various eating disorders. In obese patients, leptin dysregulation plays a significant role in the progression of obesity, while in anorexia nervosa, it illustrates its involvement in the complex neuroendocrine dysregulation associated with the disorder. Additionally, in binge eating disorder (BED), leptin dysregulation reinforces the compulsive eating behaviours characteristic of the condition. In bulimia nervosa, leptin's role in appetite regulation may also be disrupted, further contributing to the cycle of bingeing and purging behaviours. Together, these findings highlight leptin's vital function in both the physiological responses to fasting and its broader impact on eating behaviours and decision-making processes across different eating disorders.

The existing literature underscores the critical role of ghrelin and leptin in regulating hunger, satiety, and higher-order decision-making processes, with their dysregulation contributing to various eating disorders. However, there is a limited body of research examining the effects of dietary macronutrients on ghrelin and leptin, as well as their effects on eating disorders, particularly in relation to how these macronutrients might influence the hormonal regulation of appetite and energy homeostasis.

7. CONCLUSION

The nuanced relationship between ghrelin and leptin highlights their pivotal roles in appetite regulation, energy homeostasis, and behavioural responses to dietary composition. While extensive research has underscored the significant role of ghrelin and leptin in eating disorders, considerable gaps remain in understanding how dietary macronutrients influence the regulation of these hormones, particularly in relation to sex differences. While some studies suggest that carbohydrates are effective in suppressing ghrelin and proteins enhance leptin sensitivity, these findings are not consistently explored across different eating disorder subtypes. Future research should focus on elucidating the precise mechanisms through which macronutrients influence these hormones and their subsequent effects on appetite, satiety, and reward pathways. Furthermore, ghrelin and leptin hold promise as biomarkers for early diagnosis and as potential therapeutic targets. A deeper exploration of these factors could lead to more effective treatments for eating disorders, ultimately enhancing patient outcomes.

AUTHORSHIP CONTRIBUTION STATEMENT

Balqis Mohd Mazlan: writing – original draft; Farah Hanis: writing – original draft; Nik Ahmad Nizam Nik Malik: writing – review and editing; Mohd Aizuddin Mohd Lazaldin: writing – review and editing; Maheza Irna Mohamad Salim: conceptualization, supervision, writing – review and editing.

DATA AVAILABILITY

Data are available within the article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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