REVIEW ARTICLE

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Obesity and its effects on the endocrine system – a narrative review

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Abstract

Introduction and Objective. Obesity is a chronic multifactorial disease associated with metabolic and endocrine disturbances affecting multiple hormonal pathways. Excess dysfunctional adipose tissue contributes to chronic low-grade inflammation, insulin resistance, neuroendocrine dysregulation, and hormonal imbalance. The aim of this narrative review is to evaluate the impact of obesity on the endocrine system, emphasising metabolic, reproductive, thyroid, stress-related, and appetite-regulating hormones.

Review Methods. A narrative review was conducted using PubMed, Scopus, and Google Scholar databases. Publications concerning obesity-related endocrine dysfunction, adipokines, insulin resistance, thyroid and reproductive hormones, hypothalamic-pituitary-adrenal axis disturbances, and appetite-regulating hormones were analyzed. Original studies, meta-analyses, and clinically relevant reviews published mainly in recent years were included.

Brief description of the state of knowledge. Obesity-related endocrine dysfunction involves altered leptin and adiponectin signaling, insulin resistance, cortisol metabolism changes, thyroid-stimulating hormone abnormalities, and dysregulation of ghrelin and glucagon-like peptide-1. Excess adiposity affects multiple hormonal axes and is associated with reproductive dysfunction, including polyendocrine metabolic ovarian syndrome, obesity-related hypogonadism, and impaired fertility. Many endocrine abnormalities may improve after weight reduction achieved through lifestyle intervention, pharmacotherapy, or bariatric surgery.

Summary. Obesity should be regarded not only as excessive fat accumulation, but also as a condition characterized by widespread endocrine dysregulation. Understanding hormonal mechanisms involved in obesity may support earlier identification of endocrine complications and more individualized therapeutic strategies.

Key words

obesity, endocrine system, HPA axis, appetite regulation, metabolic hormones, hormonal

INTRODUCTION AND OBJECTIVE

Adipose tissue is no longer regarded only as a passive energy storage compartment, but as an active endocrine organ that secretes adipokines, cytokines and hormones involved in appetite regulation, glucose metabolism, inflammation, and reproductive function. Dysregulated secretion of leptin, adiponectin, resistin, and pro-inflammatory mediators contributes to chronic low-grade inflammation and metabolic imbalance. In particular, altered leptin-adiponectin signalling is associated with adipose tissue inflammation, insulin resistance, and increased cardiometabolic risk [1–6].

The endocrine consequences of obesity result from complex interactions between peripheral metabolic signals and central neuroendocrine regulation. Excess adiposity affects the hypothalamic-pituitary-thyroid, hypothalamic-pituitary-gonadal, and hypothalamic-pituitary-adrenal axes, contributing to hormonal disturbances that may further exacerbate weight gain and metabolic dysfunction. Obesity-related endocrine dysregulation may also impair fertility in both women and men through mechanisms involving insulin resistance, inflammation, and altered steroid hormone metabolism [7, 8].

Appetite regulation is also altered in obesity due to disturbances in gut-derived hormones and neuroendocrine signalling pathways [7]. Ghrelin and glucagon-like peptide-1 (GLP-1) play important roles in hunger and satiety regulation, while obesity is associated with impaired sensitivity to these regulatory mechanisms. Advances in understanding gut-brain axis signaling have contributed to the development of modern anti-obesity therapies, particularly incretin-based pharmacological strategies [9–11].

Importantly, weight reduction achieved through lifestyle modification, pharmacotherapy or bariatric surgery, may partially reverse obesity-associated hormonal disturbances. Improvements in insulin sensitivity, adipokine secretion, reproductive hormone profiles, thyroid function, and appetite-regulating hormone secretion have been observed after significant weight loss, highlighting the dynamic nature of endocrine dysfunction in obesity [1, 2, 7,8].

Obesity should therefore be considered not only a metabolic disorder, but also a condition characterized by extensive endocrine dysregulation. The aim of this review is to summarise current evidence regarding the impact of

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obesity on the endocrine system, with particular emphasis on metabolic hormones, thyroid function, reproductive hormones, stress-related endocrine pathways, and appetite-regulating hormones. The review also aims to discuss the clinical significance of these hormonal alterations and their relevance to weight reduction, pharmacotherapy, and bariatric surgery.

Review methods. Publications focusing on obesity-related endocrine disturbances, metabolic hormones, reproductive endocrine dysfunction, thyroid function, stress-related hormonal pathways, and appetite-regulating hormones were included. Original studies, meta-analyses, systematic reviews, and clinically relevant review articles published mainly within the last eight years were prioritized. Older publications were included only when they provided important background information or widely cited evidence relevant to the topic. Articles not directly related to obesity-associated endocrine dysfunction, publications without accessible full text or sufficient bibliographic data, conference abstracts, and non-English papers were excluded.

Because this article is a narrative review, no formal systematic review protocol or quantitative meta-analysis was performed. The selected literature was analyzed thematically and organized according to the main endocrine pathways affected by obesity.

DESCRIPTION OF THE STATE OF KNOWLEDGE

Metabolic hormones and obesity. Obesity is associated with disturbances in metabolic hormone regulation caused by excessive adipose tissue accumulation and chronic low-grade inflammation. Adipose tissue secretes hormones and signalling molecules that regulate appetite, insulin sensitivity, glucose metabolism, lipid homeostasis, and inflammatory responses. In individuals with obesity, dysregulated adipokine secretion and altered endocrine signalling contribute to insulin resistance and metabolic complications [1, 2].

Leptin and adiponectin are among the most important adipokines involved in obesity-related metabolic dysfunction. Leptin is mainly produced by white adipose tissue and regulates appetite and energy expenditure through hypothalamic pathways. Under physiological conditions, leptin suppresses food intake and promotes energy utilization. In obesity, chronically elevated leptin concentrations are often accompanied by leptin resistance, which reduces central responsiveness to leptin signalling. As a result, appetite suppression becomes impaired despite increased adipose tissue mass and high circulating leptin levels [1, 7, 12].

Leptin resistance is also linked to systemic inflammation and impaired insulin sensitivity. Excess adipose tissue increases secretion of pro-inflammatory cytokines, including tumour necrosis factor-alpha and interleukin-6, which interfere with insulin signalling and promote metabolic dysregulation. Persistent hyperleptinaemia may therefore worsen obesity-related insulin resistance and cardiometabolic risk [1, 2, 12]. Furthermore, leptin exerts critical peripheral effects that are highly relevant to obesity management and its complications, including the direct modulation of lipolysis in adipose tissue, and the regulation of blood pressure through vascular mechanisms [13, 14].

Adiponectin has anti-inflammatory, insulin-sensitising, and antiatherogenic properties. Unlike leptin, its circulating concentrations are usually reduced in obesity. Low adiponectin levels are associated with impaired glucose metabolism, insulin resistance, visceral adiposity, chronic inflammation, and endothelial dysfunction [1, 2, 15]. The adiponectin-leptin ratio has been proposed as a functional marker of adipose tissue dysfunction and metabolic inflammation, as a lower ratio reflects worsening insulin resistance and increased metabolic risk [1, 2].

Insulin resistance is one of the central endocrine abnormalities in obesity. Visceral fat accumulation impairs insulin signalling in skeletal muscle, adipose tissue, and the liver. Increased release of free fatty acids from dysfunctional adipose tissue promotes ectopic lipid accumulation and further reduces insulin responsiveness [16]. Compensatory hyperinsulinaemia may maintain glucose homeostasis initially, but prolonged insulin resistance can progress to impaired glucose tolerance and type 2 diabetes mellitus [12, 15].

Obesity is also associated with reduced spontaneous growth hormone secretion and impaired pulsatile release, particularly in abdominal obesity. This may contribute to visceral adiposity, reduced lipolysis, impaired lipid metabolism, and worsening insulin sensitivity. Weight reduction achieved through lifestyle intervention, pharmacotherapy, or bariatric surgery may improve insulin sensitivity, adipokine secretion, and systemic inflammation, while incretin-based therapies may provide additional metabolic benefits through appetite suppression and improved glucose metabolism [7, 15, 17, 18].

Sex hormones and metabolic dysregulation in obesity. Obesity affects reproductive endocrine function in both women and men through mechanisms involving insulin resistance, chronic inflammation, adipokine imbalance, and altered hypothalamic-pituitary-gonadal axis activity. Excess adipose tissue disturbs sex hormone synthesis, metabolism, and signalling, increasing the risk of infertility, hypogonadism, and metabolic reproductive disorders [19–27].

In women, obesity is strongly associated with polyendocrine metabolic ovarian syndrome (PMOS), a common endocrine disorder characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology [35, 36]. PMOS is frequently accompanied by insulin resistance and metabolic abnormalities. Obesity worsens PMOS by promoting compensatory hyperinsulinaemia, which stimulates ovarian androgen production and suppresses hepatic sex hormone-binding globulin synthesis. This increases free androgen levels and contributes to menstrual irregularities, infertility, and metabolic dysfunction [19–21].

Visceral adiposity is particularly important in the pathophysiology of PMOS. Abdominal fat accumulation is associated with greater insulin resistance, chronic inflammation, and impaired adipokine secretion. Elevated leptin and reduced adiponectin levels may further disrupt ovarian function and steroidogenesis, contributing to reproductive and metabolic abnormalities [20–22]. Hyperinsulinaemia may enhance luteinizing hormone-mediated androgen synthesis in ovarian theca cells and impair follicular maturation, increasing the risk of metabolic syndrome, dyslipidaemia, and type 2 diabetes mellitus in women with PMOS [20–24].

Therapeutic approaches targetting obesity and insulin resistance may improve reproductive and metabolic outcomes in PMOS. Weight reduction can improve ovulatory function, decrease androgen concentrations, and enhance insulin sensitivity. GLP-1 receptor agonists have also shown promising effects on body weight and metabolic parameters in women with obesity-related PMOS [23, 24].

In men, obesity is commonly associated with hypogonadism, reduced testosterone levels, and impaired reproductive function. Excess adipose tissue increases aromatase activity, promoting peripheral conversion of testosterone to estradiol. Elevated estrogen levels may suppress hypothalamic gonadotropin-releasing hormone secretion and reduce luteinizing hormone stimulation of testicular testosterone production, resulting in secondary hypogonadism [25–27].

Chronic inflammation and insulin resistance may additionally impair Leydig cell function and testosterone synthesis. Low testosterone is associated with visceral adiposity, reduced muscle mass, worsening insulin resistance, and adverse metabolic outcomes, creating a self-perpetuating cycle between obesity and hypogonadism [25–27]. Obesity may also impair semen quality by reducing sperm concentration and motility and by increasing oxidative stress, inflammation, and hormonal imbalance [25, 26].

Weight reduction can partially reverse obesity-associated reproductive endocrine dysfunction. Improvements in insulin sensitivity, visceral adiposity, and inflammation may restore gonadal hormone balance and improve fertility-related parameters. In men, substantial weight loss has been associated with increased testosterone concentrations, supporting the reversible nature of obesity-related hypogonadism [27].

Thyroid hormones and obesity. Obesity is associated with alterations in thyroid hormone metabolism and hypothalamic-pituitary-thyroid axis regulation. Excess adipose tissue may influence thyroid hormone secretion, thyroid-stimulating hormone (TSH) concentrations, peripheral hormone metabolism, and thyroid autoimmunity. These changes may contribute to metabolic dysregulation and complicate obesity-related disorders [28–34].

One of the most common thyroid-related findings in obesity is mildly elevated TSH with normal free thyroxine levels. This pattern is often observed in euthyroid individuals with obesity and may represent an adaptive response to increased energy expenditure rather than primary hypothyroidism. However, true sub-clinical hypothyroidism is also frequently documented in patients with obesity and metabolic syndrome, presenting a distinct diagnostic challenge in clinical practice [37]. Elevated leptin levels may stimulate hypothalamic thyrotropin-releasing hormone production and increase pituitary TSH secretion. Chronic inflammation and altered peripheral thyroid hormone metabolism may also affect hypothalamic-pituitary-thyroid axis regulation [28, 31–33].

Thyroid hormones regulate basal metabolic rate, thermogenesis, lipid metabolism, and glucose homeostasis. Even subtle changes in thyroid function may therefore influence body weight and metabolic health. Increased TSH concentrations in obesity have been associated with higher body mass index, visceral adiposity, insulin resistance, and dyslipidaemia, suggesting close interaction between thyroid function and metabolic dysfunction [15, 28, 33].

Obesity has also been linked to increased thyroid autoimmunity. Excess adipose tissue promotes chronic inflammation and immune activation through adipokines and pro-inflammatory cytokines, which may contribute to autoimmune thyroid disease. Increased prevalence of thyroid autoantibodies and autoimmune thyroiditis in individuals with obesity supports the concept that obesity-related inflammation may influence thyroid immune regulation [28].

Many obesity-associated thyroid abnormalities appear to be at least partially reversible after weight reduction. Lifestyle interventions and bariatric surgery have been associated with lower TSH concentrations and improved thyroid hormone profiles. These observations suggest that elevated TSH in obesity may often represent a functional and reversible endocrine adaptation rather than permanent thyroid disease [29–33].

Bariatric surgery may also influence thyroid hormone absorption and levothyroxine requirements. Anatomical and physiological changes after surgical procedures can alter drug absorption and metabolism, affecting treatment in patients with hypothyroidism. Careful monitoring of thyroid function is therefore recommended after bariatric surgery, particularly in individuals receiving thyroid hormone replacement therapy [34].

Stress hormones and the hypothalamic-pituitary-adrenal axis in obesity. Obesity is associated with altered regulation of stress-related endocrine pathways, particularly the hypothalamic-pituitary-adrenal (HPA) axis. The HPA axis maintains metabolic homeostasis and coordinates physiological responses to stress through regulation of cortisol secretion. Chronic activation or dysregulation of this system may contribute to obesity, insulin resistance, visceral adiposity, and metabolic syndrome [8, 38–41].

Under physiological conditions, HPA axis activation leads to hypothalamic secretion of corticotropin-releasing hormone, pituitary release of adrenocorticotropic hormone, and cortisol production by the adrenal cortex. Cortisol affects glucose metabolism, lipid storage, appetite regulation, inflammatory responses, and energy balance. Persistent disturbances in cortisol secretion may therefore promote metabolic abnormalities commonly observed in obesity [8, 38–41].

Visceral obesity is closely associated with abnormalities in cortisol metabolism and HPA axis activity. Excess cortisol exposure promotes adipocyte differentiation and preferential fat accumulation in visceral adipose tissue. Visceral adiposity further contributes to insulin resistance, dyslipidemia, hypertension, and chronic inflammation, creating a bidirectional relationship between obesity and HPA axis dysfunction [8, 40, 41].

Although obesity has traditionally been associated with hypercortisolism, cortisol regulation in obesity appears more complex. Some individuals with obesity may show lower basal serum cortisol despite increased free cortisol availability and altered tissue-specific cortisol metabolism. Enhanced peripheral cortisol turnover and changes in glucocorticoid metabolism may contribute to these findings [39, 40].

Altered cortisol dynamics may also involve circadian rhythm disturbances and abnormal stress responsiveness. Chronic metabolic stress, inflammation, sleep disorders, and psychosocial stressors can impair HPA axis feedback mechanisms. Dysregulated cortisol patterns may contribute

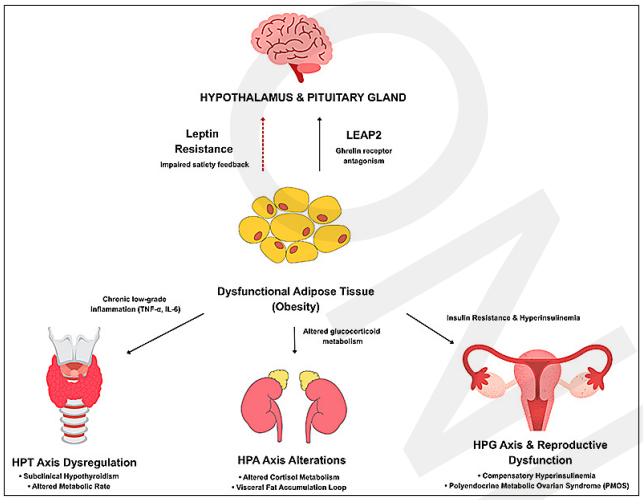

Figure 1. Central and peripheral neuroendocrine axis alterations in obesity. Dysfunctional adipose tissue drives chronic low-grade inflammation, insulin resistance, and altered glucocorticoid metabolism, leading to disruptions in the hypothalamic-pituitary-thyroid (HPT) axis (sub-clinical hypothyroidism), hypothalamic-pituitary-adrenal (HPA) axis, and hypothalamic-pituitary-gonadal (HPG) axis, accelerating polyendocrine metabolic ovarian syndrome (PMOS). At the central level, leptin resistance and elevated LEAP2 levels disrupt homeostatic metabolic signaling.
Source: Created by the authors using Canva based on references [1–16]

to appetite dysregulation, emotional eating, impaired glucose metabolism, and worsening insulin resistance [38–41].

Hair cortisol concentration has emerged as a biomarker of long-term cortisol exposure and chronic stress. Increased hair cortisol levels have been associated with overweight and obesity, supporting the relationship between chronic stress-related endocrine dysregulation and adiposity. Inflammation and adipokine imbalance may further alter HPA axis regulation by stimulating central stress pathways and modifying glucocorticoid receptor sensitivity [2, 8, 38–41].

Obesity-related HPA axis dysfunction may contribute not only to metabolic complications but also to psychological disturbances, including anxiety, depression, and chronic stress-related disorders. Weight reduction may partially improve HPA axis regulation through improvements in insulin sensitivity, inflammation, sleep quality, and metabolic health, although reversibility may vary depending on the duration and severity of endocrine dysregulation [38–41].

Appetite-regulating hormones and obesity. Appetite regulation depends on interactions between peripheral hormones, gastrointestinal signalling, adipose tissue-derived mediators, and central nervous system pathways. In obesity, disturbances in appetite-regulating hormones contribute to impaired satiety signalling, excessive energy intake, altered energy balance, and difficulty maintaining weight loss. Dysregulation of gut-brain axis communication is therefore a major mechanism in obesity and an important therapeutic target [7, 42–46].

The hypothalamus integrates peripheral signals related to hunger, satiety, nutrient availability, and adipose tissue mass. Hormones released from the gastrointestinal tract and adipose tissue influence neuronal pathways responsible for appetite stimulation and suppression. In obesity, chronic overnutrition and hormonal resistance impair normal responsiveness to these regulatory systems [7, 42, 43].

Ghrelin, produced mainly by the stomach, is a key appetite-regulating hormone. Its secretion increases before meals and stimulates appetite through hypothalamic orexigenic pathways. Ghrelin also promotes food-seeking behaviour, adiposity, and energy conservation. Circulating ghrelin concentrations are often lower in individuals with obesity than in normal weight individuals, which may reflect chronic positive energy balance and adaptive endocrine changes. However, appetite regulation remains impaired due to central resistance and dysregulated satiety signaling [42, 44, 45]. This central resistance is increasingly attributed to the dysregulation of the LEAP2 (liver-expressed antimicrobial peptide 2) system; in obesity, elevated LEAP2 levels act as a non-competitive antagonist of the ghrelin receptor, directly impairing physiological ghrelin signaling and hunger-satiety coordination [47, 48].

Bariatric surgery significantly affects ghrelin and gut hormone signalling. Sleeve gastrectomy removes a large portion of ghrelin-producing gastric tissue and is associated with reduced circulating ghrelin levels, while Roux-en-Y gastric bypass also profoundly alters post-surgical ghrelin dynamics and fundus functionality [49]. These changes may contribute to appetite suppression and sustained weight loss, although the metabolic benefits of bariatric procedures involve multiple endocrine mechanisms beyond ghrelin reduction alone [44–46].

GLP-1 is another major appetite-regulating hormone involved in glucose metabolism and satiety. It is secreted by intestinal L cells in response to nutrient intake and promotes insulin secretion, delays gastric emptying, suppresses glucagon release, and enhances satiety. In obesity, impaired GLP-1 signaling and altered incretin responses may contribute to overeating and metabolic dysfunction [7, 43]. GLP-1 receptor agonists reduce appetite, decrease energy intake, improve insulin sensitivity, and promote substantial weight loss. They may also improve obesity-associated endocrine disturbances, including reproductive dysfunction and insulin resistance [23, 24, 43].

Additional gut-derived hormones, including peptide YY, cholecystokinin, oxyntomodulin, and gastric inhibitory peptide, and amylin, participate in appetite regulation and energy homeostasis [50]. Interactions between these hormones, central reward pathways, and adipokines create an integrated neuro-endocrine network controlling feeding behaviour. Obesity is associated with impaired sensitivity to satiety signals and dysregulated reward-related eating, which complicates appetite control [7, 42, 43].

Weight loss interventions may induce significant changes in appetite-related hormone responses. Altered fasting and postprandial gut hormone secretion after lifestyle modification, pharmacotherapy, or bariatric surgery can influence long-term weight maintenance. Endocrine adaptations that increase hunger after weight reduction may partly explain frequent weight regain. Appetite regulation is also closely connected with leptin signalling, insulin resistance, stress-related hormones, and inflammation [1, 2, 7, 8, 12, 38, 42].

Clinical implications and therapeutic perspectives. Obesity-related endocrine abnormalities have important clinical consequences for metabolic health, cardiovascular risk, reproductive function, and quality of life. Dysregulation of adipokines, insulin signalling, thyroid hormones, appetite-

regulating hormones, stress-related pathways, and gonadal function contributes to obesity-associated complications. Understanding these mechanisms is important for early diagnosis, risk assessment, and individualized treatment planning [1, 2, 7, 8, 12, 19–27, 38–43].

Insulin resistance is a key endocrine consequence of obesity and links excess adiposity with type 2 diabetes mellitus, metabolic syndrome, and cardiovascular disease. Chronic inflammation, altered adipokine secretion, and compensatory hyperinsulinemia impair glucose metabolism and increase cardiometabolic risk. Early recognition of these disturbances may help prevent long-term complications [1, 2, 12, 15].

Reproductive endocrine dysfunction is also clinically relevant. In women, obesity may worsen PMOS, menstrual disorders, infertility, and metabolic complications. In men, excess adiposity is associated with hypogonadism, reduced testosterone levels, impaired semen quality, and adverse metabolic outcomes. Weight reduction may improve reproductive hormone profiles in both sexes [19–27].

Thyroid abnormalities in obesity require careful interpretation. Mildly elevated TSH may reflect adaptive and reversible changes rather than primary thyroid disease. Weight loss may improve thyroid hormone profiles; however, patients receiving levothyroxine after bariatric surgery require monitoring because altered absorption may affect dose requirements [28–34].

Table 1. Therapeutic approaches targeting endocrine dysfunction in obesity

Intervention	Main endocrine effects
Lifestyle modification	Improved insulin sensitivity and adipokine profile
GLP-1 receptor agonists	Appetite suppression, weight reduction
Bariatric surgery	Improved gut hormone signalling and metabolic profile
Endoscopic procedures	Partial reversal of hormonal disturbances through gastric volume restriction

Modern obesity treatment increasingly targets endocrine mechanisms of appetite regulation and metabolic dysfunction. GLP-1 receptor agonists reduce appetite, support weight loss, improve glycaemic control, and may positively influence obesity-associated hormonal disturbances. Bariatric surgery remains the most effective treatment for severe obesity and produces metabolic benefits through weight reduction and changes in gut hormone signalling [23, 24, 34, 43–46].

Despite therapeutic progress, long-term obesity management remains challenging because neuroendocrine adaptations may promote hunger, reduced energy expenditure, and weight regain. Effective treatment should combine lifestyle modification, pharmacotherapy, bariatric surgery when indicated, and long-term monitoring of endocrine and metabolic complications [1, 2, 7, 8, 12, 15, 23, 24, 42, 43].

SUMMARY

A central mechanism linking obesity with endocrine dysfunction is chronic low-grade inflammation combined with insulin resistance and adipokine imbalance. Altered leptin and adiponectin signalling contributes to impaired glucose metabolism, increased cardiometabolic risk, and disturbed hypothalamic appetite regulation. These abnormalities interact with the hypothalamic-pituitary-gonadal, hypothalamic-pituitary-thyroid, and hypothalamic-pituitary-adrenal axes, creating a bi-directional relationship in which obesity promotes hormonal disturbances, while endocrine dysfunction may further contribute to weight gain and metabolic deterioration.

The reviewed evidence indicates that obesity has important clinical consequences for both women and men. In women, excess adiposity is associated with PMOS, menstrual irregularities, insulin resistance, hyperandrogenism, and impaired fertility. In men, obesity may contribute to hypogonadism, reduced testosterone concentrations, impaired semen quality, and adverse metabolic outcomes. Thyroid function may also be affected, most commonly through mild and often reversible increases in TSH.

Appetite-regulating hormones and gut-brain axis signaling play a key role in obesity development and persistence. Disturbances in ghrelin, GLP-1, and other gastrointestinal hormones contribute to impaired hunger and satiety regulation, excessive energy intake, and difficulty maintaining weight loss. The clinical relevance of these mechanisms is reflected in the effectiveness of incretin-based therapies, particularly GLP-1 receptor agonists, which improve body weight, appetite control, insulin sensitivity, and selected endocrine abnormalities.

Many hormonal disturbances associated with obesity appear to be at least partially reversible after effective weight reduction. Lifestyle intervention, pharmacotherapy, and bariatric surgery may improve insulin sensitivity, adipokine secretion, reproductive hormone profiles, thyroid function, appetite-regulating hormone responses, and systemic inflammation. Nevertheless, long-term management remains challenging because neuroendocrine adaptations promoting hunger, reduced energy expenditure, and weight regain may persist after weight loss.

Overall, obesity should be understood not only as excessive fat accumulation, but also as widespread endocrine dysfunction affecting multiple physiological systems. Recognition of these hormonal mechanisms may

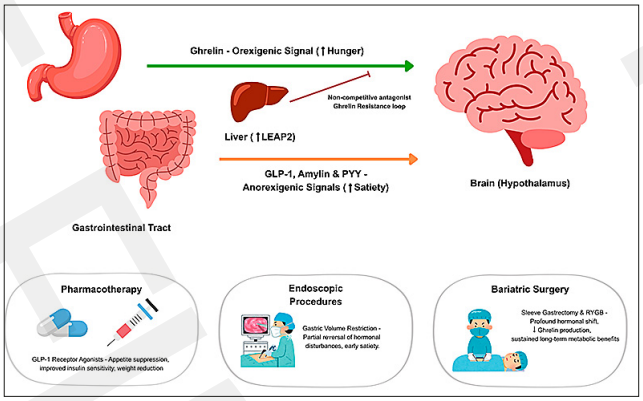

Figure 2. Gut-brain axis dysregulation and therapeutic interventions in obesity. The upper panel illustrates the hormonal communication between the gastrointestinal tract and the central nervous system, highlighting the disruptive role of liver-derived LEAP2 as a ghrelin receptor antagonist (driving ghrelin resistance) alongside altered satiety signaling (GLP-1, Amylin, PYY). The lower panel outlines how contemporary therapeutic modalities – pharmacotherapy, endoscopic procedures and bariatric surgery, target these specific physiological pathways to restore metabolic signalling and support weight reduction.
Source: Created by the authors using Canva based on references [42–50]

support earlier identification of complications and improve individualized treatment strategies. Further research should focus on defining endocrine profiles in patients with obesity and developing targetted approaches addressing both metabolic and hormonal aspects of the disease.

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