International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	NEUROIMMUNOLOGICAL AND METABOLIC CORRELATION: A MULTIDIMENSIONAL REVIEW OF THE LINKS BETWEEN OBESITY AND ANXIETY DISORDERS
DOI	https://doi.org/10.31435/ijitss.2(50).2026.5163
RECEIVED	06 March 2026
ACCEPTED	01 June 2026
PUBLISHED	17 June 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

NEUROIMMUNOLOGICAL AND METABOLIC CORRELATION: A MULTIDIMENSIONAL REVIEW OF THE LINKS BETWEEN OBESITY AND ANXIETY DISORDERS

Julia Wawerska *(Corresponding Author, Email: julia.wawerska@gmail.com)*
Medical University of Lodz, Łódź, Poland
ORCID ID: 0009-0006-0145-6204

Martyna Grzywacz
Medical University of Lodz, Łódź, Poland
ORCID ID: 0009-0002-4366-4379

Łukasz Deska
10th Military Clinical Hospital with Independent Public Healthcare Centre Polyclinic in Bydgoszcz, Bydgoszcz, Poland
ORCID ID: 0009-0009-9593-7077

Balbina Tybulczuk
Medical University of Lublin, Lublin, Poland
ORCID ID: 0000-0002-2854-4697

Agata Kaczmarzyk
Medical University of Lodz, Łódź, Poland
ORCID ID: 0009-0005-7448-9827

Weronika Zarzycka
1st Military Clinical Hospital with the Outpatient Clinic, al. Racławickie 23, 20-049 Lublin, Poland
ORCID ID: 0009-0004-1927-4076

Jakub Skrzypek
Stefan Cardinal Wyszyński Provincial Specialist Hospital SPZOZ in Lublin, Al. Kraśnicka 100, 20-718 Lublin, Poland
ORCID ID: 0009-0004-1155-5818

Natalia Fidut
Stefan Cardinal Wyszyński Provincial Specialist Hospital SPZOZ in Lublin, Al. Kraśnicka 100, 20-718 Lublin, Poland
ORCID ID: 0009-0006-2550-3933

Karol Szyprowski
1st Military Clinical Hospital with the Outpatient Clinic, al. Racławickie 23, 20-049 Lublin, Poland
ORCID ID: 0009-0001-0336-6425

Kamila Zioło
1st Military Clinical Hospital with the Outpatient Clinic, al. Racławickie 23, 20-049 Lublin, Poland
ORCID ID: 0009-0003-3875-4000

ABSTRACT

Contemporary clinical medicine faces two global health crises: obesity and anxiety disorders. Although historically treated as independent entities, contemporary epidemiology points to a clear correlation between them – the risk of anxiety disorders in obese individuals is significantly higher. The aim of this systematic review of the literature is to provide a comprehensive, multi-level analysis of the mechanisms linking excess body weight to anxiety disorders. The study hypothesises the existence of a "metabolic-anxiety vicious circle" mediated by chronic inflammation, hypothalamic-pituitary-adrenal axis dysfunction, and gut-brain axis disorders. An extensive review was conducted in the PubMed, Scopus, Web of Science and Google Scholar databases, covering publications from 2000 to 2025. The selection included cohort studies (e.g., NEMESIS-2, LifeLines), meta-analyses, and translational studies. Analysis of the scientific evidence allows us to identify four key pathophysiological pillars. Firstly, visceral obesity generates chronic low-grade inflammation, which induces neuroinflammation in limbic structures through the blood-brain barrier. Secondly, chronic anxiety leads to dysregulation of the hypothalamic-pituitary-adrenal axis and hypercortisolemia, causing visceral obesity. Thirdly, genetic variants have pleiotropic effects. Fourthly, intestinal dysbiosis is a new key mediator in the communication between metabolism and the psyche. Obesity and anxiety are not coincidental co-occurring phenomena, but are manifestations of a common dysregulation of the body's homeostasis. This implies the need to change existing treatment patterns to an integrated model that combines somatic treatment with psychotherapeutic treatment.

KEYWORDS

Obesity, Anxiety Disorders, Systemic Inflammation, HPA Axis, Gut Microbiota, Psychosomatics

CITATION

Julia Wawerska, Martyna Grzywacz, Łukasz Deska, Balbina Tybulczuk, Agata Kaczmarzyk, Weronika Zarzycka, Jakub Skrzypek, Natalia Fidut, Karol Szyprowski, Kamila Zioło. (2026) Neuroimmunological and Metabolic Correlation: a Multidimensional Review of the Links Between Obesity and Anxiety Disorders. *International Journal of Innovative Technologies in Social Science*. 2(50). doi: 10.31435/ijitss.2(50).2026.5163

1. Introduction

The World Health Organisation (WHO) warns that obesity is a global problem and its prevalence is steadily increasing. In 1990, 25% of adults were overweight (including obese), and by 2022, this figure was estimated at 43%, representing 2.5 billion adults, including more than 890 million people suffering from obesity. In 2022, 1 in 8 people were obese. Defined as abnormal or excessive fat accumulation (BMI ≥ 30 kg/m^2), obesity is no longer seen as merely an aesthetic problem or the result of a lack of willpower, but has become a recognised chronic, recurrent disease with a complex aetiology. At the same time, anxiety disorders – including generalised anxiety disorder (GAD), panic disorder, social anxiety disorder (SAD) and agoraphobia – are the most common group of mental disorders. The co-occurrence of these two conditions – metabolic and mental – creates the phenomenon of anxious obesity, which poses a diagnostic and therapeutic challenge far greater than the sum of its parts. Patients with a dual diagnosis have a poorer prognosis, lower quality of life, greater resistance to pharmacological treatment and a higher risk of cardiovascular complications [17]. In recent years, there has been an evolution of paradigms. For much of the 20th century, the myth of the "jolly fat hypothesis" prevailed in medicine and psychology, popularised, among others, by the works of Crisp and McGuiness [7]. This hypothesis assumed that obese people, thanks to their allegedly lower neurotic sensitivity and hedonistic approach to life, are protected from anxiety disorders. Overeating was interpreted as an effective defence mechanism reducing emotional tension. Contemporary science has verified this view. The breakthrough came with the discovery of the endocrine function of adipose tissue and the identification of leptin by Jeffrey M. Friedman in 1994. Based on contemporary scientific reports, we know that obesity is a state of chronic systemic inflammation that strongly correlates with anxiety disorders. A meta-analysis by Luppino et al. [16] showed that there is a bidirectional relationship between these two conditions: the risk of obesity was 58% higher in people with depression, while the risk of depression in obese people was 55% higher.

Aim and scope of the study

This paper provides a comprehensive review of the literature from 2000 to 2025, aiming to summarise the available scientific evidence on the relationship between obesity and anxiety disorders. Unlike standard reviews, this article integrates the psychiatric and diabetological perspectives, with a particular emphasis on the latest reports on molecular mechanisms (the role of pro-inflammatory cytokines, gut microbiota) and genetic mechanisms (twin studies and GWAS). The aim of the study is to provide clinicians with hard evidence for the need for a holistic approach to the patient, in which the treatment of anxiety is an indispensable part of obesity therapy.

2. Materials and Methods

The literature review was conducted in accordance with the standards for systematic reviews, adapting the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to the narrative form of an expert review. The following electronic databases were searched: PubMed/MEDLINE, Scopus, Web of Science, PsycINFO and Cochrane Library. The review covers the period from 1 January 2000 to 31 March 2025, which allowed for the inclusion of the latest studies published just before the finalisation of this manuscript. Case reports, editorial articles without new data, and studies on specific populations not related to the general mechanism (e.g., obesity in rare genetic syndromes) were excluded.

Artificial intelligence tools were used in this study solely as supporting instruments under the supervision of the authors. They were used to translate selected fragments of the manuscript, correct scientific language (text clarity, grammar, style) and streamline data processing.

At no stage did AI replace the authors' decisions or substantive assessments.

3. Results

3.1 Epidemiology and Prevalence

Analysis of epidemiological data provides indisputable evidence that the relationship between obesity and anxiety is not a statistical artefact, but a real clinical phenomenon with global reach.

3.1.1 Prospective cohort studies: Evidence for causality

The strongest evidence for the direction of the relationship is provided by long-term observational studies. Particular attention should be paid to the NEMESIS-2 (Netherlands Mental Health Survey and Incidence Study-2) study, cited by Leonore de Wit et al. [2]. In this study, a representative sample of 5,303 Dutch adults aged 18-64 were observed over a period of 3 years. The key finding was that individuals who were obese (BMI $\geq$ 30) at baseline had a significantly increased risk of developing anxiety disorders during the follow-up period. Another fundamental study is the LifeLines Cohort Study, discussed by Nigatu et al. [17]. This study, involving a group of 89,332 participants, drew attention to the interaction between obesity, abdominal obesity and anxiety disorders in the context of health-related quality of life (HRQL). A synergistic negative effect was demonstrated: individuals suffering from both abdominal obesity and anxiety disorders experienced a significantly more severe decline in physical and social functioning than would be expected from simply adding up the effects of both conditions. This means that anxiety in an obese person is more devastating to daily functioning than anxiety in a person of normal weight.

3.1.2 The role of body composition and fat distribution

Contemporary epidemiology is moving away from the simple BMI index in favour of body composition analysis. Guedes et al.[26] in a study of patients with metabolic syndrome showed that it was not so much total body weight as the percentage of fat mass that correlated positively with the severity of anxiety symptoms ($r = 0.30$, $p = 0.039$). Another observation was a strong inverse correlation between lean body mass and anxiety ($r = -0.57$, $p < 0.0001$). This suggests that total lean mass, and thus muscle tissue, may have a protective function (probably through the secretion of myokines with anti-inflammatory and neuroprotective effects), while adipose tissue has a pro-inflammatory effect.

3.1.3 Population specificity: Psychiatric patients

This relationship is even more dramatic in the population of people with diagnosed mental illnesses. A meta-analysis conducted by Medhia Afzal et al. [8], covering 120 studies from 43 countries, showed that people with mental disorders have a more than 3-fold higher risk of obesity (OR = 3.04) compared to the general population. The prevalence of obesity in people with mental disorders was 25.9%, and overweight and obesity as high as 60.1%. This indicates systemic neglect of somatic health in this group of patients and the iatrogenic effect of certain psychotropic drugs, which will be discussed later in this paper.

3.2 Pathophysiological Mechanisms

3.2.1 Chronic inflammation

A fundamental discovery of the last two decades is the definition of obesity as a state of chronic low-grade inflammation. Inflammation in obesity differs from its acute form, in particular by the absence of typical symptoms characteristic of inflammation (rubor, calor, dolor, tumour, functio laesa), and its effects are long-lasting and systemic. The adipose tissue of obese individuals, especially visceral fat, is penetrated by macrophages, which change their phenotype from anti-inflammatory M2 to pro-inflammatory M1. This leads to the overproduction of cytokines: Interleukin-6 (IL-6), tumour necrosis factor alpha (*TNF-α*) and Interleukin-1 beta (*IL-1β*), leptin and resistin. Markers of inflammation in obesity correlate more effectively with waist circumference and waist-to-hip ratio than with BMI. As indicated by Castanon, Lasselin and Capuron [9] and Capuron and Miller [30], these cytokines do not remain only at the periphery, but modulate neural circuits, neurochemistry and behaviour. They have the ability to affect the brain through five main mechanisms:

1. Passage through leaky areas of the blood-brain barrier
2. Active transport via specific transporters
3. Activation of endothelial cells to release other signalling molecules, e.g. prostaglandins and nitric oxide
4. Transmission of cytokine signals via sensory nerves, e.g. the vagus nerve
5. Entry into the brain parenchyma of peripherally activated monocytes. [30]

Once they reach the brain, inflammatory signals activate microglia – the brain's immune cells. Activated microglia produce cytokines in situ, leading to neuroinflammation in key structures that regulate emotions: the amygdala (anxiety centre), hippocampus (emotional memory) and prefrontal cortex (executive function). The molecular mechanism of this effect involves the induction of the enzyme indoleamine 2,3-dioxygenase (IDO). IDO degrades tryptophan, a precursor of serotonin, redirecting it to the kynurenine pathway. This results in the formation of neurotoxic metabolites (e.g. quinolinic acid and 3-hydroxykynurenine), which act as agonists on NMDA receptors, causing excitotoxicity and anxiety symptoms. A decrease in serotonin levels as a result of impaired tryptophan metabolism due to inflammation is one of the well-documented mechanisms of drug resistance in anxiety disorders in obese individuals [32].

3.2.2 Hypothalamic-Pituitary-Adrenal (HPA) Axis: Hormonal Feedback

The HPA axis is the body's main adaptive system in response to stress. Under physiological conditions, stress activates the hypothalamus to secrete corticotropin-releasing hormone (CRH), which stimulates the pituitary gland to produce ACTH, which in turn stimulates the adrenal cortex to release cortisol. Cortisol, through negative feedback, should inhibit further activity of the axis. In anxiety disorders and obesity, this inhibitory mechanism is impaired.

Hypercortisolemia and visceral obesity: Chronic anxiety is associated with persistently elevated cortisol levels. As explained by Bose et al. [4] in their paper, visceral adipose tissue has a much higher density of glucocorticoid receptors (GR) than subcutaneous fat. Cortisol activates lipoprotein lipase (LPL) in visceral adipocytes, promoting fat accumulation within the abdominal cavity. This results in the formation of a so-called "stress belly".

Glucocorticoid resistance: Cheng et al. [5] showed that obese patients with anxiety experience glucocorticoid receptor resistance (GR resistance). Despite high cortisol levels, the signal to suppress inflammation does not reach the immune cells. This leads to a paradoxical situation: high cortisol and high inflammation at the same time.

The role of leptin: Aschbacher et al. [14] emphasise the role of leptin, a satiety hormone secreted by adipose tissue. Under physiological conditions, leptin inhibits the HPA axis, reducing the stress response. However, obese individuals are leptin-resistant. The brain does not recognise leptin, resulting in a lack of HPA axis inhibition and chronic anxiety.

3.2.3 Gut-Brain Axis

The most dynamically developing area of research is the role of the gut microbiota. The gut and brain influence each other via the vagus nerve, immune and neuroendocrine pathways. In their article, Luo et al. [13] shed new light on this mechanism. The "Western" diet (high in fat and sugar), typical of obesity development, leads to drastic changes in the composition of the microbiota (dysbiosis): a decrease in the number of beneficial Bifidobacterium and Lactobacillus bacteria and an increase in Firmicutes bacteria. Dysbiosis has two key effects on anxiety:

Leaky gut syndrome: Disruption of the integrity of the intestinal barrier allows the translocation of bacterial lipopolysaccharides (LPS) into the bloodstream. LPS is a potent endotoxin that triggers a systemic inflammatory response, secondarily exacerbating neuroinflammation and anxiety.

Neurotransmitter production: Gut bacteria are responsible for the production of precursors to many neurotransmitters. [31]

3.2.4 Genetics and pleiotropy.

Molecular genetics research suggests that both conditions result from the same genetic predisposition. Key evidence comes from a study by Walter et al. [12], which analysed variants of the FTO (Fat Mass and Obesity-associated) gene. This gene is the strongest known genetic determinant of obesity. The researchers found that certain polymorphisms of the FTO gene are correlated not only with high BMI, but also with the risk of phobic anxiety, regardless of the body weight of the subjects. This points to the phenomenon of pleiotropy – one gene influences two seemingly unrelated phenotypic traits. This is supported by twin studies [21], which show that genetic factors explain a significant part of the covariance between obesity and internalising mental disorders. Kennedy et al. [29] used voxel-based morphometry (VBM) in twins to show that shared genes influence brain structure in areas responsible for regulating appetite and emotions (amygdala, orbitofrontal cortex). This means that some patients are born with a neurobiological predisposition to overeat in response to stress and to experience excessive anxiety.

3.3 Psychological and Behavioural Dimensions: The Vicious Circle of Addiction and Anxiety

While biological mechanisms (inflammation, cortisol, genes) form the basis for the simultaneous development of obesity and anxiety, psychological and behavioural factors play a major role in maintaining this pathological condition on a daily basis. An analysis of the literature allows us to identify specific behavioural phenotypes that bridge the gap between psychiatry and somatic medicine.

3.3.1 Emotional dysregulation and the phenomenon of "emotional eating"

A key psychological construct linking anxiety and obesity is a deficit in emotion regulation. Henriques et al. [28] in a study of 612 adults showed that the relationship between BMI and anxiety symptoms is not direct:

1. Difficulties in emotion regulation (DERS): Patients with high levels of anxiety have a reduced ability to tolerate psychological distress (distress tolerance).
2. Avoidant coping styles: Instead of confronting the *source* of anxiety, the patient "escapes" into substitute behaviours.
3. Emotional eating: This is an adaptive (coping) mechanism in which food consumption serves to regulate affective tension rather than satisfy physiological hunger.

The neurobiological mechanism behind this phenomenon is fascinating. The consumption of high-carbohydrate and high-fat foods ("comfort food") stimulates the reward system (nucleus accumbens) to release dopamine and endogenous opioids, which brings immediate, albeit short-lived, relief from anxiety (the anxiolytic effect of food). At the same time, insulin facilitates the transport of tryptophan to the brain, temporarily raising serotonin levels. For patients with chronic anxiety, food becomes the most readily available and fastest-acting "sedative". Unfortunately, this leads to a calorie surplus and secondary guilt, which generates another wave of anxiety and closes the vicious circle.

3.3.2 Anxiety Sensitivity and Chronic Pain

Obesity is one of the most stigmatised conditions in modern society. Vorokhta and Bieliaieva [19] demonstrated in a clinical study that patients with abdominal obesity and migraine have a 1.8 times higher risk of anxiety disorders with panic attacks and a 1.5 times higher risk of phobic anxiety. One of the key mechanisms underlying this phenomenon is Weight Bias Internalisation (WBI), which involves patients accepting negative stereotypes about obesity and applying them to themselves. This process leads to a significant decrease in self-esteem and an increase in anxiety symptoms. In order to avoid situations that trigger anxiety and panic attacks, patients often give up socialising and group physical activities, which further exacerbates their weight problems. A study by Yokoyama et al.[25] points to significant links between body image dissatisfaction and mental functioning in overweight and obese individuals. The authors showed that the level of dissatisfaction with body image correlates with the severity of anxiety symptoms, and that this relationship is reciprocal and dynamic during cognitive-behavioural therapy. Although the level of anxiety was not an independent predictor of improved body image, the results suggest that anxiety may co-occur with negative body image and indirectly influence avoidance behaviours. In this context, social anxiety may promote avoidance of social exposure situations, such as using the gym, swimming pool or eating in public places, leading to isolation and increasing the risk of overeating alone, and ultimately to weight gain.

3.3.3 Sleep disorders: A night-time anxiety generator

Obesity is one of the most important risk factors for the development of obstructive sleep apnoea (OSA), which leads to sleep fragmentation and recurrent episodes of nocturnal hypoxia. These disorders result in excessive activation of the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis, which promotes increased secretion of catecholamines and cortisol and morning fatigue and emotional tension. A study by Mazzitelli et al. showed that sleep quality is an independent correlate of anxiety symptom severity, highlighting the important role of sleep disorders in modulating patients' mental state [11]. Furthermore, it has been suggested that chronic hypoxia and sleep disorders may be associated with dysregulation of neurotransmitters involved in mood regulation, including serotonin, but these relationships remain the subject of further research and do not allow for clear cause-and-effect conclusions [22]. The relationship between obesity, obstructive sleep apnoea and anxiety should therefore be viewed as a complex, multifactorial pathophysiological model in which metabolic, neuroendocrine and psychological mechanisms coexist.

3.4 Therapeutic Interventions: From Theory to Clinical Practice

The complexity of pathomechanisms (biological and psychological) implies the need for multimodal therapy. Monotherapy rarely produces lasting effects.

3.4.1 Cognitive Behavioural Therapy (CBT): The gold standard

CBT is currently the best-documented form of psychotherapy for the treatment of both anxiety disorders and obesity in the form of CBT-OB. A recent randomised controlled trial (RCT) published in 2025 by Cassin et al. [18] in the journal *Obesity Surgery* provided groundbreaking data. In the study, patients who had undergone bariatric surgery who received telephone-based CBT (Tele-CBT) showed a significant reduction in generalised anxiety symptoms (GAD-7 scale: -3.2 points) compared to the control group, and these effects persisted for 18 months. CBT in this model did not focus solely on diet, but included:

- **Cognitive restructuring:** identification and modification of "sabotaging thoughts" and anxiety catastrophising,
- **Exposure:** gradual familiarisation with anxiety-provoking situations (e.g. eating in company, wearing tight-fitting clothes) without resorting to overeating,
- **Problem solving:** learning adaptive methods of coping with stress.
- Research also indicates that personalised CBT-OB protocols that address obesity-specific issues such as body dysmorphic disorder and perfectionism are more effective [6, 20]. Anxiety reduction during therapy is an important predictor of weight loss success – patients with lower anxiety levels are more consistent in changing their eating habits and lifestyle.

3.4.2. Third Wave CBT: Mindfulness and ACT

Emma R Lawlor et al. [24] point to the growing role of third wave therapies, particularly Acceptance and Commitment Therapy (ACT) and Mindfulness (MBCT), in their systematic review. Mindfulness training helps patients distinguish between physiological and emotional hunger and observe waves of anxiety without immediately responding to them with food (so-called urge surfing). Lappalainen et al. [3] have proven that web-guided mindfulness interventions are effective in reducing both BMI and psychological distress.

3.4.3. Pharmacotherapy: Challenges and new opportunities

The pharmacological treatment of patients with obesity and anxiety requires precision to avoid iatrogenic effects.

Psychotropic trap: Many classic anti-anxiety and mood-stabilising drugs (e.g. olanzapine, quetiapine, pregabalin, some SSRIs such as paroxetine) cause significant weight gain by increasing appetite and causing metabolic changes. Afzal et al. [8] point to this as a very important cause of obesity in the psychiatric population.

Neutral/beneficial drugs: If pharmacotherapy for anxiety is necessary in an obese person, first-line drugs should be those with a neutral profile (e.g. bupropion – although with caution in anxiety, vortioxetine, duloxetine) or sertraline/fluoxetine (at higher doses they can reduce appetite).

The GLP-1 revolution: The greatest hope in recent years is GLP-1 receptor agonists (semaglutide, liraglutide, tirzepatide). Although registered for the treatment of diabetes and obesity, they have a central effect. By influencing the reward system and the nucleus accumbens, they not only suppress hunger, but can also reduce compulsive behaviour and "emotional hunger". Preliminary clinical observations suggest improved mood and reduced anxiety in patients treated with GLP-1, which may result from both direct neurotropic effects and indirectly from weight loss and reduced inflammation.

3.4.4. Bariatric interventions and mental health

Bariatric surgery is currently considered the most effective treatment for morbid obesity. In their work, Huai Henga Loha et al. [27] point to a significant reduction in the incidence of anxiety symptoms in the postoperative period – the percentage of patients with these symptoms decreased to 16.9% (95% CI 0.12–0.22), with an odds ratio (OR) of 0.58 (95% CI 0.51–0.67; $p < 0.001$). In addition, a significant improvement in anxiety symptoms assessed using the HADS scale was observed. The mean score in the anxiety component decreased from 7.66 ± 0.99 before surgery to 6.16 ± 1.18 after surgery. Further analysis showed that the postoperative BMI obtained had an impact on the reduction of anxiety symptoms. In the group of patients with a postoperative BMI of ≥35 kg/m², the percentage of individuals with anxiety symptoms decreased from 25.4% before surgery to 20.9% after surgery (OR = 0.72; 95% CI 0.60–0.86; $p = 0.0003$). In contrast, among patients with a postoperative BMI <35 kg/m², the percentage of individuals with anxiety symptoms decreased from 33.3% to 21.3%. Cassin and Park [18] warn that without psychological support (e.g. Tele-CBT), some patients experience weight gain after 12-18 months without behavioural changes, which in turn drives drug use and a vicious circle. The phenomenon of "addiction transfer" (replacing food with alcohol or drugs) is a real threat as a self-regulatory mechanism in patients after surgical treatment. [33]

3.4.5. The role of physical activity in the multi-level modulation of mental health

Regular physical activity has a significant impact on the functioning of the central nervous system and the regulation of inflammatory processes, which play a key role in the pathophysiology of anxiety disorders. As indicated by data from a literature review, physical exercise leads to increased expression of brain-derived neurotrophic factor (BDNF), which supports neurogenesis, synaptogenesis and neuron survival, especially in the hippocampus – a structure involved in the regulation of emotions and stress responses "Incorporating exercise into treatment plans alongside conventional therapies has the potential to reduce mortality without introducing the side effects commonly associated with pharmacological treatment"[16].

4. Discussion

The literature review allows us to formulate a coherent theoretical model that integrates the data collected so far. Obesity and anxiety disorders are not separate diseases that happen to occur in the same patient. Rather, they are two manifestations of the same profound disturbance of the body's homeostasis, involving dysregulation of the immune, endocrine and nervous systems. The "Vicious Circle of Obesity and Anxiety" identified in this study operates on the principle of positive feedback. Psychological stress and anxiety activate the HPA axis, thereby increasing cortisol levels, which promotes the accumulation of visceral fat. Visceral fat generates pro-inflammatory cytokines, causing inflammation throughout the body and in the central nervous system. Inflammation exacerbates anxiety symptoms, partly through the activation of the kynurenine pathway, leading to the formation of neurotoxic metabolites that modulate neurotransmission. Anxiety further drives behavioural coping mechanisms such as overeating, which increases body weight. Weight gain exacerbates gut dysbiosis and social stigmatisation, which in turn increases anxiety levels, creating a vicious cycle.

The current healthcare model, based on narrow specialised fields, is ineffective in the face of this complex problem. Psychiatrists should routinely monitor metabolic parameters (waist circumference, lipid profile) and treat dietary interventions and health education as elements of anxiety treatment equivalent to pharmacotherapy. Ignoring obesity in an anxious patient means ignoring a significant source of inflammation that sustains mental disorders. Primary care physicians and diabetologists should routinely monitor obese patients for anxiety disorders using tools such as the GAD-7 scale. Untreated anxiety disorders are a common cause of weight loss failure.

Despite advances in knowledge, there is still a lack of long-term intervention studies evaluating the effectiveness of combination therapy (e.g., simultaneous administration of GLP-1 drugs and CBT psychotherapy) compared to monotherapy. Another intriguing area of research is the influence and mechanism of action of the gut-brain axis on anxiety reduction in obese individuals.

5. Conclusions

There is a strong, statistically and clinically significant correlation between obesity and anxiety disorders. The risk is bidirectional, but stronger for the impact of obesity on the development of anxiety, especially in women and people with abdominal obesity.

Common Biological Denominator: Chronic inflammation is the basis for this correlation. Visceral adipose tissue acts as an active endocrine gland secreting pro-inflammatory cytokines that modulate brain metabolism.

HPA Axis and Microbiota: Dysregulation in the HPA axis and gut microbiota disorders (gut-brain axis) are key pathophysiological pathways mediating this relationship.

Effective treatment requires an integrated approach. Psychotherapy, particularly cognitive behavioural therapy (CBT), should be standard in the treatment of obesity, and weight and inflammation control should be standard in the treatment of anxiety. Promising results are being achieved with new forms of therapy: Tele-CBT (increasing accessibility) and incretin drugs (GLP-1), which may be the missing pharmacological link between metabolism and the psyche. In light of the information gathered, we believe that integrated medicine should be the starting point for assessing clinical status and selecting treatment methods for patients. Looking at things through a narrow prism is insufficient due to the multifactorial aetiopathogenesis of diseases such as obesity and anxiety disorders.

Author Contributions:

Conceptualization: Julia Wawerska, Martyna Grzywacz, Weronika Zarzycka
Methodology: Agata Kaczmarzyk, Łukasz Deska, Balbina Tybulczuk
Software: Jakub Skrzypek, Natalia Fidut, Karol Szyprowski
Investigation: Julia Wawerska, Martyna Grzywacz
Resources: Kamila Zioło, Jakub Skrzypek, Balbina Tybulczuk, Karol Szyprowski, Natalia Fidut
Data Curation: Łukasz Deska, Kamila Zioło
Writing – Original Draft Preparation: Karol Szyprowski, Jakub Skrzypek, Łukasz Deska
Writing – Review & Editing: Balbina Tybulczuk, Agata Kaczmarzyk
Visualization: Balbina Tybulczuk, Natalia Fidut
Supervision: Martyna Grzywacz, Weronika Zarzycka
Project Administration: Julia Wawerska

All authors have read and approved the final version of the manuscript.

Funding: The study did not receive external funding.

Conflicts of interest: The authors declare no conflicts of interest.

Statement on the use of generative AI and AI-assisted tools in the writing process: In preparing this work, the authors used Gemini 3.0 to assist in translating selected sections of the manuscript and to improve the language, style, and clarity of the text. After using the tool, the authors fully reviewed and edited the content and bear sole responsibility for the substantive content of the publication.

REFERENCES

1. Kauffman, B. Y., Rogers, A. H., Garey, L., & Zvolensky, M. J. (2022). Anxiety and depressive symptoms among adults with obesity and chronic pain: The role of anxiety sensitivity. *Cognitive Behaviour Therapy, 51*(4), 295–308. https://doi.org/10.1080/16506073.2021.2011396
2. de Wit, L., ten Have, M., Cuijpers, P., & de Graaf, R. (2022). Body mass index and risk for onset of mood and anxiety disorders in the general population: Results from the Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2). *BMC Psychiatry, 22*, Article 522. https://doi.org/10.1186/s12888-022-04077-w
3. Lappalainen, R., Sairanen, E., Järvelä, E., Rantala, S., Korpela, R., Puttonen, S., Kujala, U. M., Myllymäki, T., Peuhkuri, K., Mattila, E., Kaipainen, K., Ahtinen, A., Karhunen, L., Pihlajamäki, J., Järnefelt, H., Laitinen, J., Kutinlahti, E., Saarelma, O., Ermes, M., & Kolehmainen, M. (2014). The effectiveness and applicability of different lifestyle interventions for enhancing wellbeing: The study design for a randomised controlled trial for persons with metabolic syndrome risk factors and psychological distress. *BMC Public Health, 14*, Article 310. https://doi.org/10.1186/1471-2458-14-310
4. Bose, M., Oliván, B., & Laferrère, B. (2009). Stress and obesity: The role of the hypothalamic–pituitary–adrenal axis in metabolic disease. *Current Opinion in Endocrinology, Diabetes and Obesity, 16*(5), 340–346. https://doi.org/10.1097/MED.0b013e32832fa137

5. Cheng, T., Dimitrov, S., Pruitt, C., & Hong, S. (2016). Glucocorticoid-mediated regulation of inflammation in human monocytes is associated with depressive mood and obesity. *Psychoneuroendocrinology, 66*, 195–204. https://doi.org/10.1016/j.psyneuen.2016.01.008
6. Dalle Grave, R., Sartirana, M., & Calugi, S. (2020). Personalised cognitive-behavioural therapy for obesity (CBT-OB): Theory, strategies and procedures. *BioPsychoSocial Medicine, 14*, Article 5. https://doi.org/10.1186/s13030-020-00177-9
7. Crisp, A. H., & McGuiness, B. (1976). Jolly fat: Relation between obesity and psychoneurosis in general population. *British Medical Journal, 1*, 7–9. https://doi.org/10.1136/bmj.1.6000.7
8. Afzal, M., Siddiqi, N., Ahmad, B., Afsheen, N., Aslam, F., Ali, A., Ayesha, R., Bryant, M., Holt, R., Khalid, H., Ishaq, K., Koly, K. N., Rajan, S., Saba, J., Tirbhowan, N., & Zavala, G. A. (2021). Prevalence of overweight and obesity in people with severe mental illness: Systematic review and meta-analysis. *Frontiers in Endocrinology, 12*, Article 769309. https://doi.org/10.3389/fendo.2021.769309
9. Castanon, N., Lasselin, J., & Capuron, L. (2014). Neuropsychiatric comorbidity in obesity: Role of inflammatory processes. *Frontiers in Endocrinology, 5*, Article 74. https://doi.org/10.3389/fendo.2014.00074
10. Hallihan, H., Tsai, P., Lv, N., Xiao, L., Bernabé, B. P., Wu, Y., Pandey, G. N., Williams, L. M., Ma, J., & Ajilore, O. A. (2023). Affective neural circuits and inflammatory markers linked to depression and anxiety symptoms in patients with comorbid obesity. *Journal of Psychiatric Research, 160*, 9–18. https://doi.org/10.1016/j.jpsychires.2023.01.044
11. Mazzitelli, M., Trunfio, M., Milinković, A., Castelli, E., Sasset, L., Leoni, D., Salvucci, M., Cazzaro, R., Calcinoni, I., Balducci, P., Ribeiro, G. C. Q., Filagrana, G., Scaglione, V., & Cattelan, A. M. (2023). Sleep disturbances and their correlation with cardiovascular risk, obesity, and mood disorders in people with HIV. *AIDS, 37*(6), 925–934. https://doi.org/10.1097/QAD.0000000000003493
12. Walter, S., Glymour, M. M., Koenen, K., Liang, L., Tchetgen Tchetgen, E. J., Cornelis, M., Chang, S.-C., Rewak, M., Rimm, E., Kawachi, I., & Kubzansky, L. D. (2015). Do genetic risk scores for body mass index predict risk of phobic anxiety? Evidence for a shared genetic risk factor. *Psychological Medicine, 45*(1), 181–191. https://doi.org/10.1017/S0033291714001226
13. Luo, K., Zhang, M., Tu, Q., Li, J., Wang, Y., Wan, S., Li, D., Qian, Q., & Xia, L. (2025). From gut inflammation to psychiatric comorbidity: Mechanisms and therapies for anxiety and depression in inflammatory bowel disease. *Journal of Neuroinflammation, 22*(1), Article 149. https://doi.org/10.1186/s12974-025-03476-6
14. Aschbacher, K., Rodriguez-Fernandez, M., van Tmarschen, H., Tomiyama, A. J., Jain, S., Epel, E., Doyle, F. J., III, & van der Greef, J. (2014). The hypothalamic–pituitary–adrenal–leptin axis and metabolic health: A systems approach to resilience, robustness and control. *Interface Focus, 4*(5), Article 20140020. https://doi.org/10.1098/rsfs.2014.0020
15. Romero Garavito, A., Díaz Martínez, V., Juárez Cortés, E., Negrete Díaz, J. V., & Montilla Rodríguez, L. M. (2025). Impact of physical exercise on the regulation of brain-derived neurotrophic factor in people with neurodegenerative diseases. *Frontiers in Neurology, 15*, Article 1505879. https://doi.org/10.3389/fneur.2024.1505879
16. Luppino, F. S., de Wit, L. M., Bouvy, P. F., Stijnen, T., Cuijpers, P., Penninx, B. W. J. H., & Zitman, F. G. (2010). Overweight, obesity, and depression: A systematic review and meta-analysis of longitudinal studies. *Archives of General Psychiatry, 67*(3), 220–229. https://doi.org/10.1001/archgenpsychiatry.2010.2
17. Nigatu, Y. T., Reijneveld, S. A., de Jonge, P., van Rossum, E., & Bültmann, U. (2016). The combined effects of obesity, abdominal obesity and major depression/anxiety on health-related quality of life: The LifeLines Cohort Study. *PLOS ONE, 11*(2), Article e0148871. https://doi.org/10.1371/journal.pone.0148871
18. Cassin, S. E., Park, K., Leung, S. E., Ma, C., Tomlinson, G., Hawa, R., Wnuk, S., Jackson, T., Urbach, D., Okrainec, A., Brown, J., Sandre, D., & Sockalingam, S. (2025). A randomised-controlled trial examining telephone-based cognitive behavioural therapy for patients after metabolic and bariatric surgery: 18-month follow-up results. *Obesity Surgery, 35*, 4103–4113. https://doi.org/10.1007/s11695-025-08163-2
19. Vorokhta, Y. M., & Bieliaieva, N. V. (2023). Structure of anxiety disorders in patients with chronic migraine and abdominal obesity. *Clinical and Preventive Medicine*, (8), 52–58. https://doi.org/10.31612/2616-4868.8.2023.06
20. dos Santos Moraes, A., da Costa Padovani, R., La Scala Teixeira, C. V., Soria Cuesta, M. G., dos Santos Gil, S., de Paula, B., dos Santos, G. M., Gonçalves, R. T., Dâmaso, A. R., Oyama, L. M., Gomes, R. J., & Caranti, D. A. (2021). Cognitive behavioural approach to treat obesity: A randomised clinical trial. *Frontiers in Nutrition, 8*, Article 611217. https://doi.org/10.3389/fnut.2021.611217
21. Campbell, A. C., Calais-Ferreira, L., Hahn, E., Spinath, F. M., Hopper, J. L., & Young, J. T. (2024). Familial confounding of internalising symptoms and obesity in adolescents and young adults: A co-twin analysis. *International Journal of Obesity, 48*, 876–883. https://doi.org/10.1038/s41366-024-01491-w
22. Tkachenko, V., & Bagro, T. (2023). The correlation between body weight, serotonin levels, mental health status, sleep disorders and metabolism in patients with obesity. *International Journal of Endocrinology (Ukraine), 19*(5), 354–362. https://doi.org/10.22141/2224-0721.19.5.2023.1299

23. Savulescu-Fiedler, I., Mihalcea, R., Dragosloveanu, S., Scheau, C., Baz, R. O., Caruntu, A., Scheau, A.-E., Caruntu, C., & Benea, S. N. (2024). The interplay between obesity and inflammation. *Life, 14*(7), Article 856. https://doi.org/10.3390/life14070856
24. Lawlor, E. R., Islam, N., Bates, S., Griffin, S. J., Hill, A. J., Hughes, C. A., Sharp, S. J., & Ahern, A. L. (2020). Third-wave cognitive behaviour therapies for weight management: A systematic review and network meta-analysis. *Obesity Reviews, 21*(7), Article e13013. https://doi.org/10.1111/obr.13013
25. Yokoyama, H., Nozaki, T., Nishihara, T., Sawamoto, R., Komaki, G., & Sudo, N. (2022). Factors associated with the improvement of body image dissatisfaction of female patients with overweight and obesity during cognitive behavioural therapy. *Frontiers in Psychiatry, 13*, Article 1025946. https://doi.org/10.3389/fpsyt.2022.1025946
26. Guedes, E. P., Madeira, E., Mafort, T. T., Madeira, M., Moreira, R. O., Mendonça, L. M., Godoy-Matos, A. F., Lopes, A. J., & Farias, M. L. F. (2013). Body composition and depressive/anxiety symptoms in overweight and obese individuals with metabolic syndrome. *Diabetology & Metabolic Syndrome, 5*, Article 82. https://doi.org/10.1186/1758-5996-5-82
27. Loh, H. H., Francis, B., Lim, L. L., Yee, A., & Loh, H. S. (2021). Improvement in mood symptoms after post-bariatric surgery among people with obesity: A systematic review and meta-analysis. *Diabetes/Metabolism Research and Reviews, 37*(8), Article e3458. https://doi.org/10.1002/dmrr.3458
28. Henriques, J., Afreixo, V., Unterrainer, H., & Senra, H. (2025). Psychological mediators of the association between obesity and symptoms of depression, anxiety, and stress. *Neuropsychobiology, 84*(1), 26–37. https://doi.org/10.1159/000542767
29. Kennedy, J. T., Astafiev, S. V., Golosheykin, S., Korucuoglu, O., & Anokhin, A. P. (2019). Shared genetic influences on adolescent body mass index and brain structure: A voxel-based morphometry study in twins. *NeuroImage, 199*, 261–272. https://doi.org/10.1016/j.neuroimage.2019.05.053
30. Capuron, L., & Miller, A. H. (2011). Immune system to brain signalling: Neuropsychopharmacological implications. *Pharmacology & Therapeutics, 130*(2), 226–238. https://doi.org/10.1016/j.pharmthera.2011.01.014
31. Noble, E. E., Hsu, T. M., & Kanoski, S. E. (2017). Gut to brain dysbiosis: Mechanisms linking Western diet consumption, the microbiome, and cognitive impairment. *Frontiers in Behavioral Neuroscience, 11*, Article 9. https://doi.org/10.3389/fnbeh.2017.00009
32. Almutabagani, L. F., Almanqour, R. A., Alsabhan, J. F., Alhossan, A. M., Alamin, M. A., Alrajeh, H. M., Alonazi, A. S., El-Malky, A. M., & Alrasheed, N. M. (2023). Inflammation and treatment-resistant depression from clinical to animal study: A possible link? *Neurology International, 15*(1), 100–120. https://doi.org/10.3390/neurolint15010009
33. Scheen, A. J. (2025). Weight loss therapy and addiction: Increased risk after bariatric surgery but reduced risk with GLP-1 receptor agonists. *Diabetes & Metabolism, 51*(2), Article 101612. https://doi.org/10.1016/j.diabet.2025.101612