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The Relationship Between Obesity and Depressive Disorders: Biological Mechanisms and Clinical Implications - A Narrative Review

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Abstract

Introduction

Obesity and depressive disorders are among the most prevalent chronic conditions worldwide. Increasing evidence suggests a bidirectional relationship between obesity and depression. Their coexistence is associated with a higher risk of metabolic diseases, poorer clinical outcomes, and reduced quality of life. In recent years, growing attention has been focused on the biological mechanisms underlying this association.

Methods

A narrative review of the literature was conducted using the PubMed and Scopus databases. The search included publications published between 2011 and 2025. Clinical studies, systematic reviews, and meta-analyses addressing the biological mechanisms linking obesity and depression were included.

Results

Available evidence indicates that obesity increases the risk of developing depression, while depression may contribute to weight gain through lifestyle changes and neuroendocrine disturbances. The key biological mechanisms include chronic low-grade inflammation, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, alterations in neurotransmitter systems, and changes in the gut–brain axis associated with the gut microbiota.

Conclusions

A better understanding of the pathophysiological mechanisms linking obesity and depression may contribute to the development of more effective therapeutic strategies and improve patients' quality of life.

Keywords:

obesity; depression; chronic inflammation; hypothalamic-pituitary-adrenal axis; gut-brain axis

Introduction

Obesity represents one of the major public health challenges of the modern world, with a steadily increasing prevalence. It is estimated that more than 650 million adults worldwide are affected by obesity, and this number continues to rise, making it one of the most significant public health concerns of the 21st century. Obesity is associated with an increased risk of cardiovascular diseases, type 2 diabetes, and other metabolic disorders [1].

At the same time, depressive disorders are among the most common mental disorders and represent one of the leading causes of disability worldwide [2]. Increasing evidence indicates that obesity and depression frequently co-occur, and the relationship between them is bidirectional [3,4].
The coexistence of these conditions has important clinical implications, as patients with both obesity and depression often have poorer prognosis, a higher risk of somatic diseases, and reduced quality of life.
In recent years, increasing attention has been given to the biological mechanisms linking these disorders, including chronic inflammation, neuroendocrine dysregulation, and alterations in brain function.
Despite the growing number of studies examining the coexistence of obesity and depression, the biological mechanisms underlying this relationship remain incompletely understood.
The aim of this review is to present the current state of knowledge regarding the biological mechanisms linking obesity and depressive disorders and to discuss their clinical implications.

Methods

A narrative review of the scientific literature on the relationship between obesity and depressive disorders was conducted. The literature search was performed using the PubMed and Scopus databases.
The following keywords and their combinations were used: *obesity, depression, inflammation, hypothalamic-pituitary-adrenal axis, gut-brain axis, metabolic disorders, microbiota*. Keywords were combined using the logical operators AND and OR. Publications published between 2011 and 2025 were included. Only studies available in English were considered.
Original articles, systematic reviews, and meta-analyses addressing the biological mechanisms linking obesity and depression were included. Studies conducted in adult populations examining relationships between obesity, metabolic processes, and mood disorders were considered.
Publications not meeting the thematic criteria, studies with limited data availability, and articles published before 2011 were excluded.

Results

The literature review indicates a significant association between obesity and depressive disorders. Numerous epidemiological studies have shown that individuals with obesity have a higher risk of developing depressive symptoms compared with individuals with normal body weight. A meta-analysis by Mannan et al. demonstrated that obesity is associated with an increased risk of depression in adult populations [3].
Many studies suggest that the relationship between obesity and depression is bidirectional. Depression may contribute to weight gain through lifestyle changes such as reduced physical activity, sleep disturbances, and increased consumption of high-calorie foods [6].

The main findings of selected studies on the relationship between obesity and depression are presented in Table 1.

Table 1. Selected studies on the relationship between obesity and depressive disorders

Author (year)	Study type	Study objective	Study population	Main findings	Reference number
Mannan et al. (2016)	Meta-analysis	Association between obesity and depression	>50,000 participants	Obesity increases the risk of depression	[3]
Milaneschi et al. (2019)	Systematic review	Shared biological mechanisms	Adult populations	Common pathophysiological mechanisms identified	[4]
Penninx (2015)	Narrative review	Depression and metabolic disorders	Adult populations	Frequent coexistence of depression and metabolic diseases	[5]
Pan et al. (2012)	Cohort study	Direction of association	>65,000 participants	Bidirectional relationship confirmed	[6]
Miller & Raison (2016)	Narrative review	Role of inflammation	Adult populations	Inflammatory cytokines contribute to depression	[8]
Lamers et al. (2013)	Clinical study	HPA axis function	Patients with depression	HPA axis dysregulation observed	[12]
Volkow et al. (2013)	Neuroimaging study	Reward system activity	Individuals with obesity	Dopaminergic alterations observed	[13]
Cryan & Dinan (2012)	Narrative review	Gut-brain axis	Animal and translational studies	Microbiota influences mood	[15]

Psychosocial factors also play an important role. Individuals with obesity frequently experience social stigma, reduced self-esteem, and chronic stress, which may increase the risk of mood disorders [7].

Biological mechanisms are also crucial in the pathogenesis of the coexistence of obesity and depression. Studies indicate that chronic low-grade inflammation may affect central nervous system functioning and mood regulation through its influence on neurotransmitter metabolism [8-10]. Elevated levels of inflammatory markers have been observed in both individuals with obesity and patients with depression.

Many studies also emphasize the role of dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis. Chronic activation of this axis leads to increased cortisol secretion, which may contribute to fat accumulation and the development of depressive symptoms [11,12].

Another important mechanism involves alterations in neurotransmitter systems, particularly dopaminergic and serotonergic systems. These changes may affect mood regulation, eating behavior, and reward system functioning [13,14].

Increasing evidence also highlights the importance of the gut microbiota in the pathogenesis of obesity and depression. Alterations in gut microbiota composition may influence inflammation, metabolism, and the gut–brain axis [15-17].

The key biological mechanisms linking obesity and depression are presented in Table 2.

Table 2. Biological mechanisms linking obesity and depressive disorders

Mechanism	Biological process	Clinical significance
Chronic inflammation	Increased pro-inflammatory cytokines (IL-6, TNF-α)	Effects on neurotransmitter metabolism and mood regulation
HPA axis dysregulation	Increased cortisol secretion	Disturbances in stress response and metabolism
Neurotransmitter alterations	Dopaminergic and serotonergic dysfunction	Impaired mood and eating behavior
Gut microbiota	Dysbiosis, gut–brain axis disruption	Impact on inflammation and brain function

Discussion

The findings confirm a complex, multifactorial relationship between obesity and depressive disorders involving both biological and psychosocial mechanisms. Epidemiological studies indicate that individuals with obesity are at increased risk of developing depression, while depression may promote weight gain through lifestyle

changes and appetite dysregulation [3,6]. Furthermore, the coexistence of obesity and depression is often associated with metabolic disturbances such as insulin resistance and metabolic syndrome [5].

Chronic low-grade inflammation appears to be one of the key mechanisms linking obesity and depression. Adipose tissue acts as an active endocrine organ releasing pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor-alpha, which may influence brain function and neuroplasticity [8-10].

Dysregulation of the HPA axis is another important mechanism. Chronic activation of this axis leads to increased cortisol levels, which may contribute to both fat accumulation and mood disturbances [11,12].

Alterations in neurotransmitter systems, particularly dopaminergic and serotonergic pathways, also play a key role. These changes may influence mood regulation, eating behavior, and reward processing [13,14].

The gut microbiota has also emerged as an important factor. Dysbiosis may influence inflammation, metabolism, and brain function via the gut–brain axis [15-17].

From a clinical perspective, the coexistence of obesity and depression represents a significant therapeutic challenge. Patients often require a comprehensive approach combining psychiatric treatment and metabolic interventions [18]. Lifestyle modifications, including diet improvement and increased physical activity, may positively affect both metabolic health and mental well-being [19,20].

It should be noted that this review is narrative in nature, which may limit the systematic selection of studies. Despite increasing research, important gaps in knowledge remain, and further studies are needed.

Conclusions

Obesity and depressive disorders are major public health concerns that frequently coexist and interact with each other. The relationship between these conditions is bidirectional and involves both biological and psychosocial factors.

Key biological mechanisms include chronic inflammation, HPA axis dysregulation, neurotransmitter alterations, and changes in the gut microbiota. These processes affect both metabolic regulation and central nervous system function.

A better understanding of these mechanisms may contribute to the development of more effective therapeutic strategies. Future research should focus on identifying underlying mechanisms and developing integrated treatment approaches addressing both metabolic and psychiatric aspects.

Conflicts od Interest

The authors declare that they have no conflict of interest.

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Ethics Approval

Not applicable.

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