

PROSPECTS

IN PHARMACEUTICAL SCIENCES

Prospects in Pharmaceutical Sciences, 22(4), 25-30
<https://prospects.wum.edu.pl/>

Review

UNRAVELING THE WEIGHT OF EMOTIONS: A COMPREHENSIVE REVIEW OF THE INTERPLAY BETWEEN DEPRESSION AND OBESITY

Aleksandra Ziółkowska^{1*}, Szymon Wojtaszek¹, Bogdan Fels²

¹ Specialistic Municipal Hospital in Toruń, ul. Batorego 17/19, 87-100 Toruń, Poland

² Poznan University of Medical Sciences, ul. Fredry 10, 61-701 Poznań, Poland

* Correspondence, e-mail: aleksandraziolkowska315@gmail.com

Received: 24.06.2024 / Accepted: 12.08.2024 / Published: 18.10.2024

ABSTRACT

Obesity is an excessive or abnormal accumulation of fat or adipose tissue in the body. This disease impairs health in a variety of mechanisms, such as diabetes, cardiovascular disease, hypertension, hyperlipidemia, cancers, but also depression. This article aims to summarise the latest information on the correlation between depression and obesity, to make the problem more widespread, to highlight the many implications of this disease, and to encourage healthy living. Based on the existing research, we present several potential mechanisms that may link the two phenomena. Obesity and depression co-occur to a significant extent. This is linked to endocrine and immune system disorders, but also pathological psychological and social mechanisms. A review of the literature from PubMed, Google Scholar, and Medline (1996-2024) was conducted. The articles were selected based on specific keywords and then evaluated for their significance and suitability for inclusion in this review. Obesity is a complex disease leading to many health implications including depression. Treatment of both conditions is extremely important and requires a multidisciplinary approach, including pharmacological treatment, dietary counseling, psychological counseling, and lifestyle modification. Early implementation of appropriate treatment is essential to optimize treatment outcomes.

KEYWORDS: obesity; depression; weight loss.

Article is published under the CC BY license.

1. Introduction

Obesity is the excessive or abnormal accumulation of fat or adipose tissue in the body [1]. Obesity is usually defined by using weight and height to calculate "body mass index" (BMI). Healthy weight status ranges from 18.5 kg/m² to 24.9 kg/m², and overweight status ranges from 25 kg/m² to 29.9 kg/m² of BMI. A BMI that is greater than 30 kg/m² is considered to reflect obesity. According to the estimates by the World Health Organization (WHO), 39% and 13% of adults worldwide were overweight and obese, respectively, in 2014 [2]. Depression affects 280 million people worldwide [3]. The link between obesity and depression has been hypothesized and repeatedly studied. It has been confirmed. Obesity impairs health in a variety of mechanisms, such as diabetes, cardiovascular disease, hypertension, hyperlipidemia, cancers, and depression [4-7]. Obese individuals are 55% more likely to develop lifetime depression, while depressed individuals are 58% more likely to become obese compared to the general population [4]. The association of depression with obesity is higher than with overweight. This relationship is bidirectional. Depression causes weight gain, just as obesity leads to depression [9-10]. This association is explained by the effect of obesity on the HPA axis. Excess body weight dysregulates the HPA axis, and this causes depression [4,10-13]. Obesity furthermore increases

inflammation in the body, which also causes the development of depression, according to researchers [2,10,14]. Excess body weight contributes to the progression and development of diabetes. It was observed that in diabetes, changes in the brain may occur, increasing the risk of depression [4,10,15]. People with depression often adopt unhealthy lifestyles and have disturbed eating patterns which contribute to the development of obesity. In turn, obese people often suffer from pain, and chronic pain may contribute to the onset of depression [2,4,16-20]. Based on the existing research, we present several potential mechanisms that may link the two phenomena. This article aims to summarise the latest information on the correlation between depression and obesity, to make the problem more widespread, to highlight the many implications of this disease, and to encourage healthy living.

2. Materials and Methods

A review of the literature from PubMed, Google Scholar, and MedLine (1996-2024) was conducted. The articles were selected based on specific keywords, MeSH terms, and phrases such as „Depression”, „Obesity”, „Overweight”, „Correlation between depression and obesity”, „HPA and obesity”, „HPA and depression”,

„Inflammation and depression”, „Infamation and obesity”, „Association between chronic pain and obesity”, „The link between depression and chronic pain”, „Diet”, „Physical activity”, „Physical activity and depression”, „Physical activity and obesity”, „Physical activity and overweight” and then evaluated for their significance and suitability for inclusion in this review.

3. HPA

Studies show that in obesity cortisol metabolism in adipocytes is dysregulated, which leads to HPA (hypothalamic-pituitary-adrenal axis) dysregulation. Greater abdominal fat correlated with greater HPA axis reactivity, reflected in morning wakefulness and reactivity to acute stress. A marked up-regulation of cortisol secretion was observed in adipocytes (due to greater 11 β -HSD1 expression), whereas cortisol was down-regulated in liver tissue. Obesity appeared to be associated with an overreactive HPA axis in many, but not all studies [13,21].

Some studies showed under-reactivity of the axis. One study that focused on looking at the correlation between BMI (in non-obese, mildly, or severely obese populations) and peripheral cortisol values (morning blood or 24-hour urine) found no significant association. Such a correlation was also not found in any of the subgroups of obese subjects [22].

The effect of HPA dysregulation on mood disorders was studied, and it was shown that increased activity of the HPA axis is a marker of major depression. Overactive CRH neurons, secrete excessive amounts of CRH and have impaired glucocorticoid-mediated feedback. This is thought to be a hallmark of impaired neuroendocrine regulation associated with and possibly causally related to depressive disorders [12].

3.1. Inflammation

We also looked at the impact of inflammation on depression. Obesity increases inflammation. Levels of IL-5, IL-10, IL-12, IL-13, and IFN- γ are elevated in individuals with increased body weight. It is worth noting that physical activity reduces cytokine production [15,23]. Studies have shown increased levels of peripheral and central inflammatory cytokines and acute phase proteins during depression. Chronic exposure to increased inflammation causes changes in neurotransmitters and neural circuits that lead to depressive symptoms and, interestingly, may also result in reduced efficacy of antidepressants [14]. Inflammation appears to be an important mediator linking obesity and depression. This may be an important finding, for example, in patients who have a poor response to treatment.

3.2. Diet, obesity, and depression

Positive psychological changes and improvements in quality of life have been demonstrated in weight-loss individuals. Individuals who successfully lose and maintain their weight experience improvements in mood, self-confidence, and quality of life. Additionally, reductions in psychological and behavioral symptoms have been associated with increased duration of weight loss maintenance [2].

In one study, the effect of diet on psychological state was examined. The effect of a very low-carbohydrate and high-fat (LC) diet was compared with a high-carbohydrate

and low-fat (LF) diet. Improvements in mood were observed in participants in the LF group. Despite similar and significant weight loss in the LC group, once improvements were achieved in the short term, participants' mood state returned to baseline levels at the end of 1 year [24].

A number of essential nutrients are needed for healthy brain function, including vitamins, minerals, polyunsaturated fats, and amino acids, which work synergistically. Diet can modify your mood. Nutrients are required as cofactors for hundreds of different enzymes; they support metabolic pathways, neurotransmitter synthesis, cell signaling, maintenance of the myelin sheath, glucose, and lipid metabolism, mitochondrial function, prevention of oxidation, modulation of inflammatory processes, reduction of oxidative stress and modulation of the function of the hypothalamic-pituitary-adrenal axis [25-28]. Improving your overall diet will have far greater mental health benefits than any single nutrient [29].

It was shown that eating a Mediterranean diet, rich in vegetables, fruits, nuts, and legumes, can help improve mental health, reduce depression, anxiety, and stress, and increase positive emotions and relationships with the environment. It is a way of eating that not only has a positive effect on our body but also on our well-being and quality of life [25,29]. The Mediterranean diet, rich in unsaturated fats, has many health benefits. Oleate can improve glycemic control and plasma lipid profile in humans and protect against inflammation and anxiety-depressive behavior in mice. Omega-3 (n-3) polyunsaturated fatty acids, such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), are known for their anti-inflammatory properties. Increased dietary n-3 intake can improve insulin sensitivity and significantly reduce plasma CRP, interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF α) levels in humans [30].

In all the studies we reviewed, a healthy diet was associated with mental health and had a positive effect on mood. Furthermore, research shows that losing weight improves quality of life and improves mental health. Both of these factors also have a positive effect on physical health. Obese people should follow a calorie-deficit diet to lose weight, but remember to eat a diet rich in nutrients that have a positive effect on mental health, such as unsaturated fats.

3.3. Chronic Pain

Obesity leads to chronic pain. In one study, the incidence of pain in obese people was four times higher than in people who were not obese [17]. Another US study showed a linear increase in chronic pain with increasing BMI [20]. Chronic pain can lead to depression. Pain and depression are closely correlated from the perspective of both brain areas and the neurological function system [19].

Regions involved in mood regulation comprising the insular cortex, prefrontal cortex, anterior cingulate, thalamus, hippocampus, and amygdala are also active during pain, which forms a histological structural foundation for the coexistence of pain and depression [20].

3.4. Diabetes

Diabetes and depression are mutual risk factors [31-33]. Patients with diabetes are 2.5 times more likely to

develop major depression, and patients with depression are more likely to develop type 2 diabetes with an estimated relative risk of 2.2 [34-35].

Significantly lower levels of subcortical glutamate and glutamine were observed in depressed and diabetic patients [36-38]. Lower concentrations of these substances indicate the importance of glutamatergic transmission in mood disorders. Lower levels of glutamate and glutamine were associated with a lower pool of precursors in these patients. Lower precursor pools may result from a combination of impaired glucose metabolism resulting from diabetes, combined with impaired glial function, which in turn is associated with major depression [36].

Interestingly, in acute mania in patients with bipolar disorder, higher levels of Glx (glutamine/glutamate) were observed in the left dorsolateral prefrontal cortex [38-39].

It was also observed that myo-inositol levels were increased in the anterior white matter in diabetic patients with and without major depression and this was due to diabetes [36].

The studies we analyzed show that in patients with diabetes, changes occur in the functioning of brain structures. We believe that further research should focus on the mechanisms of these changes and on examining the structures that are damaged. Expanding this knowledge would allow for a more comprehensive approach to the treatment of patients with depression and diabetes. For now, it is worth preventing diabetes, one such way is to fight obesity, nutritional education, and the promotion of physical activity.

3.5. Obesity discrimination

In Europe, the ideal of beauty is a slim, shapely figure. Stores present their clothes on mannequins with idealized proportions. Despite numerous campaigns to combat obesity, overweight people still experience discrimination. Obesity, especially extreme obesity, can lead to difficulties in obtaining education, getting married, and achieving equal earnings compared to people with a healthier body weight [40]. Overweight people experience discrimination in the areas of education, work, and the health care system. People suffering from severe obesity are even more likely to experience such experiences [40-41].

The links between obesity and depression are stronger in women than in men, perhaps because of societal emphasis on thinness as an attribute of female beauty [42]. Furthermore, female adolescents with obesity are more likely to show emotional problems, depression, and anxiety [43].

We examined the relationship between everyday discrimination and depressive symptoms and suicidal thoughts during the COVID-19 pandemic. Everyday discrimination was shown to have a significant relationship with depressive symptoms and suicidal thoughts. People who experience regular discrimination have a significantly higher risk of developing moderate to severe depressive symptoms and suicidal thoughts. Moreover, this risk did not differ significantly between people diagnosed with a mood disorder before the pandemic and people who did not previously have this type of problem [44]. A recent study found that people who identified as having experienced discrimination in any area had a 46% higher risk of

developing depression compared to people who did not experience discrimination in any area of their lives [45].

3.6. The Impact of Physical Activity on Obesity and Depression

Physical activity (PA) leads to many beneficial changes in the body. The WHO recommends that all adults get at least 150-300 minutes of moderate-intensity aerobic physical activity per week (or an equivalent amount of vigorous activity) [46-47]. Almost 30% (1.4 billion) of the world's adult population do not meet recommended levels of physical activity [48]. Both aerobic and endurance training plays an important role in the treatment of obesity. As a result, there is a reduction in body fat, an increase in muscle mass, improved cardiovascular fitness, and increased bone mineral density. PA also has a beneficial effect on glucose and lipid metabolism, improving mood. It also reduces stress and improves self-esteem [49-51]. Women are more likely than men to suffer from dissatisfaction with their appearance [52].

PA improves mood through a variety of neuromolecular mechanisms. Physical activity causes the brain to produce more endogenous opioid peptides, which reduce pain and improve mood and also lead to reduced anxiety and hopelessness [46]. PA increases the expression of neurotrophic factors, increases the availability of serotonin and norepinephrine, regulates the activity of the hypothalamic-pituitary-adrenal axis, and reduces systemic inflammation [53]. Inflammation is an important mediator of the relationship between obesity, depression, and PA. PA reduces chronic inflammation induced by obesity and, as a result, reduces the risk of depression [54-55]. Regular physical activity, three times per week, has been shown to reduce all depressive episodes by 25% [48]. Furthermore, all types of PA are effective, but higher-intensity exercise is associated with greater improvement in depression and anxiety [48,53,56]. There is evidence that physical activity at a young age can provide significant predispositions in the acquisition of motor skills and positively influence perceptions of competence and self-esteem [57]. PA can contribute to current treatment protocols by acting as an adjunct to psychotherapy and pharmacotherapy [58]. Considering the broad positive health impact, 1 in 9 cases of depression could be prevented if everyone in the population were active at the level of current health recommendations [59].

One study found that exercise can also increase anxiety in overweight/obese individuals, especially if they have not been active recently. Exercise is more effective when the individual's preferences for exercise modality, mode, or intensity are taken into account [50].

Exercise helps regulate healthy eating behaviors, improves body image, and also increases patient motivation [50].

Promoting physical activity is important, but it must be done in a skillful, encouraging way. One negative example is Fitspiration. Fitspiration is a social media phenomenon that purports to inspire viewers to adopt a healthier lifestyle [60]. This content, in turn, contributes to increased body image comparison, body dissatisfaction, and negative mood among individuals, especially young adults. Results from body image measures showed that exposure to Fitspiration images increased negative mood [61].

4. Discussion/Conclusions

In summary, obesity and depression pose serious health challenges. Both diseases are widespread around the world and place a heavy burden on the healthcare system. Treatment of both diseases requires a comprehensive and multidisciplinary approach. For these reasons, obesity treatment teams should include mental health professionals who can assess and treat patients' psychological problems as needed.

There are several mechanisms linking depression with obesity, the most important of which include the endocrine system, the immune system, and psychosocial aspects. Further research is needed on the correlation between obesity and depression to understand this relationship better and thus better select therapies for patients and prevent both depression and obesity. It is important to pay attention to the co-occurrence of both diseases and treat them simultaneously if they occur together. It seems that in this specific group of patients with depression, treatment of excessive body weight may be a promising treatment method. Another very important aspect is increasing awareness of the negative effects of discrimination against overweight people and taking action to improve their social and health situation.

Physical activity has numerous health benefits, including reducing obesity, improving metabolic health, mood, and self-esteem, and reducing the risk of depression. Introducing regular exercise that is tailored to individual preferences can significantly improve the quality of life and health of the population. At the same time, promoting physical activity should be done in a way that minimizes the risk of negative effects

There is a great need for health promotion campaigns to raise awareness of the dangerous effects of depression and obesity on mental and physical health.

Author Contributions: Conceptualization, Aleksandra Ziółkowska and Szymon Wojtaszek; Methodology, Bogdan Fels and Szymon Wojtaszek; Software, Bogdan Fels and Aleksandra Ziółkowska; Check, Bogdan Fels, Szymon Wojtaszek and Aleksandra Ziółkowska; Formal analysis, Szymon Wojtaszek and Aleksandra Ziółkowska; Investigation, Bogdan Fels and Szymon Wojtaszek; Resources, Bogdan Fels and Aleksandra Ziółkowska; Data curation, Szymon Wojtaszek and Aleksandra Ziółkowska and Bogdan Fels; Writing - rough preparation, Bogdan Fels and Szymon Wojtaszek; Writing - review and editing, Szymon Wojtaszek and Aleksandra Ziółkowska; Supervision, Bogdan Fels and Aleksandra Ziółkowska; Project administration, Szymon Wojtaszek and Bogdan Fels and Aleksandra Ziółkowska. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Panuganti, K.K.; Nguyen, M.; Kshirsagar, R.K. Obesity. *StatPearls* [Internet]. 2024. Available online: <https://www.ncbi.nlm.nih.gov/books/NBK459357/> (accessed on January 2024).

2. World Health Organization. Obesity and Overweight: Fact Sheet 311. WHO 2015. Available online: <http://www.who.int/mediacentre/factsheets/fs311/en/> (accessed on 2015).
3. World Health Organization. Depressive Disorder (Depression). WHO 2023. Available online: <https://www.who.int/news-room/fact-sheets/detail/depression> (accessed on 2023).
4. Luppino, F.S.; de Wit, L.M.; Bouvy, P.F.; et al. Overweight, Obesity, and Depression: A Systematic Review and Meta-Analysis of Longitudinal Studies. *Arch. Gen. Psychiatry* 2010, 67, 220-229. doi:10.1001/archgenpsychiatry.2010.2
5. Pereira-Miranda, E.; Costa, P.R.F.; Queiroz, V.A.O.; Pereira-Santos, M.; Santana, M.L.P. Overweight and Obesity Associated with Higher Depression Prevalence in Adults: A Systematic Review and Meta-Analysis. *J. Am. Coll. Nutr.* 2017, 36, 223-233. doi:10.1080/07315724.2016.1261053
6. Faith, M.S.; Matz, P.E.; Jorge, M.A. Obesity-Depression Associations in the Population. *J. Psychosom. Res.* 2002, 53, 935-942. doi:10.1016/s0022-3999(02)00308-2
7. Frank, P.; Jokela, M.; Batty, G.D.; Lassale, C.; Steptoe, A.; Kivimäki, M. Overweight, Obesity, and Individual Symptoms of Depression: A Multicohort Study with Replication in UK Biobank. *Brain Behav. Immun.* 2022, 105, 192-200. doi:10.1016/j.bbi.2022.07.009
8. Dankel, S.J.; Loenneke, J.P.; Loprinzi, P.D. Mild Depressive Symptoms Among Americans in Relation to Physical Activity, Current Overweight/Obesity, and Self-Reported History of Overweight/Obesity. *Int. J. Behav. Med.* 2016, 23, 553-560. doi:10.1007/s12529-016-9541-3
9. Lv, N.; Kannampallil, T.; Xiao, L.; et al. Association Between User Interaction and Treatment Response of a Voice-Based Coach for Treating Depression and Anxiety: Secondary Analysis of a Pilot Randomized Controlled Trial. *JMIR Hum. Factors* 2023, 10, Art. No: e49715. 2023. doi:10.2196/49715
10. Patsalos, O.; Keeler, J.; Schmidt, U.; Penninx, B.W.J.H.; Young, A.H.; Himmerich, H. Diet, Obesity, and Depression: A Systematic Review. *J. Pers. Med.* 2021, 11, Art. No: 176. doi:10.3390/jpm11030176
11. Kurhe, Y.; Mahesh, R. Mechanisms Linking Depression Co-morbid with Obesity: An Approach for Serotonergic Type 3 Receptor Antagonist as Novel Therapeutic Intervention. *Asian J. Psychiatr.* 2015, 17, 3-9. doi:10.1016/j.ajp.2015.07.007
12. Mello, A.F.; Mello, M.F.; Carpenter, L.L.; Price, L.H. Update on Stress and Depression: The Role of the Hypothalamic-Pituitary-Adrenal (HPA) Axis. *Braz. J. Psychiatry* 2003, 25, 231-238. doi:10.1590/s1516-44462003000400010
13. Incollingo Rodriguez, A.C.; Epel, E.S.; White, M.L.; Standen, E.C.; Seckl, J.R.; Tomiyama, A.J. Hypothalamic-Pituitary-Adrenal Axis Dysregulation and Cortisol Activity in Obesity: A Systematic Review. *Psychoneuroendocrinology* 2015, 62, 301-318. doi:10.1016/j.psyneuen.2015.08.014

14. Felger, J.C. Role of Inflammation in Depression and Treatment Implications. *Handb. Exp. Pharmacol.* **2019**, *250*, 255-286. doi:10.1007/164_2018_166
15. Schmidt, F.M.; Weschenfelder, J.; Sander, C.; et al. Inflammatory cytokines in general and central obesity and modulating effects of physical activity. *PLoS One* **2015**, *10*(3): Art. No: e0121971. doi:10.1371/journal.pone.0121971
16. Okifuji, A.; Hare, B.D. The association between chronic pain and obesity. *J. Pain Res.* **2015**, *8*, 399-408. doi:10.2147/JPR.S55598
17. Hitt, H.C.; McMillen, R.C.; Thornton-Neaves, T.; Koch, K.; Cosby, A.G. Comorbidity of obesity and pain in a general population: Results from the Southern Pain Prevalence Study. *J. Pain* **2007**, *8*(5), 430-436. doi:10.1016/j.jpain.2006.12.003
18. Stone, A.A.; Broderick, J.E. Obesity and pain are associated in the United States. *Obesity (Silver Spring)* **2012**, *20*(7), 1491-1495. doi:10.1038/oby.2011.397
19. Sheng, J.; Liu, S.; Wang, Y.; Cui, R.; Zhang, X. The Link between Depression and Chronic Pain: Neural Mechanisms in the Brain. *Neural Plast.* **2017**, Art. No: 9724371. doi:10.1155/2017/9724371
20. Meerwijk, E.L.; Ford, J.M.; Weiss, S.J. Brain regions associated with psychological pain: Implications for a neural network and its relationship to physical pain. *Brain Imaging Behav.* **2013**, *7*(1), 1-14. doi:10.1007/s11682-012-9179-y
21. Cheiran Pereira, G.; Piton, E.; Moreira Dos Santos, B.; et al. Microglia and HPA axis in depression: An overview of participation and relationship. *World J. Biol. Psychiatry* **2022**, *23*(3), 165-182. doi:10.1080/15622975.2021.1939154
22. Tenk, J.; Mátrai, P.; Hegyi, P.; et al. In obesity, HPA axis activity does not increase with BMI, but declines with aging: A meta-analysis of clinical studies. *PLoS One* **2016**, *11*(11), Art. No: e0166842. doi:10.1371/journal.pone.0166842
23. Fu, X.; Wang, Y.; Zhao, F.; et al. Shared biological mechanisms of depression and obesity: Focus on adipokines and lipokines. *Aging (Albany NY)* **2023**, *15*(12), 5917-5950. doi:10.18632/aging.204847
24. Brinkworth, G.D.; Buckley, J.D.; Noakes, M.; Clifton, P.M.; Wilson, C.J. Long-term effects of a very low-carbohydrate diet and a low-fat diet on mood and cognitive function. *Arch. Intern. Med.* **2009**, *169*(20), 1873-1880. doi:10.1001/archinternmed.2009.329
25. Parletta, N.; Zarnowiecki, D.; Cho, J.; et al. A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: A randomized controlled trial (HELFIMED). *Nutr. Neurosci.* **2019**, *22*(7), 474-487. doi:10.1080/1028415X.2017.1411320
26. Staudacher, H.M.; Teasdale, S.; Cowan, C.; Opie, R.; Rocks, T.; Jacka, F.N. Diet interventions for anxiety and depression. In *Nutritional Psychiatry: A Primer for Clinicians*; Dinan, T., Ed.; Cambridge University Press: **2023**; pp. 72-100
27. Kaplan, B.J.; Crawford, S.G.; Field, C.J.; Simpson, J.S. Vitamins, minerals, and mood. *Psychol. Bull.* **2007**, *133*(5), 747-760. doi:10.1037/0033-2909.133.5.747
28. Kaplan, B.J.; Rucklidge, J.J.; Romijn, A.; McLeod, K. The Emerging Field of Nutritional Mental Health: Inflammation, the Microbiome, Oxidative Stress, and Mitochondrial Function. *Clin. Psychol. Sci.* **2015**, *3*(6), 964-980. doi:10.1177/2167702614555413
29. Parletta, N.; Milte, C.M.; Meyer, B.J. Nutritional modulation of cognitive function and mental health. *J. Nutr. Biochem.* **2013**, *24*(5), 725-743. doi:10.1016/j.jnutbio.2013.01.002
30. Fulton, S.; Décarie-Spain, L.; Fioramonti, X.; Guiard, B.; Nakajima, S. The menace of obesity to depression and anxiety prevalence. *Trends Endocrinol. Metab.* **2022**, *33*(1), 18-35. doi:10.1016/j.tem.2021.10.005
31. Osama, A.J.; Shehab, A.E.K. Psychological wellbeing and biochemical modulation in response to weight loss in obese type 2 diabetes patients. *Afr. Health Sci.* **2015**, *15*(2), 503-512. doi:10.4314/ahs.v15i2.25
32. Milano, W.; Ambrosio, P.; Carizzone, F.; et al. Depression and obesity: Analysis of common biomarkers. *Diseases* **2020**, *8*(2), Art. No: 23. doi:10.3390/diseases8020023
33. Bornstein, S.R.; Schuppenies, A.; Wong, M.L.; Licinio, J. Approaching the shared biology of obesity and depression: The stress axis as the locus of gene-environment interactions. *Mol. Psychiatry* **2006**, *11*(10), 892-902. doi:10.1038/sj.mp.4001873
34. Palinkas, L.A.; Lee, P.P.; Barrett-Connor, E. A prospective study of Type 2 diabetes and depressive symptoms in the elderly: The Rancho Bernardo Study. *Diabetic Med.* **2004**, *21*, 1185-1191. doi:10.1111/j.1464-5491.2004.01315.x
35. Eaton, W.W.; Armenian, H.; Gallo, J.; Pratt, L.; Ford, D.E. Depression and risk for onset of type II diabetes. A prospective population-based study. *Diabetes Care* **1996**, *19*(10), 1097-1102. doi:10.2337/diacare.19.10.1097
36. Ajilore, O.; Haroon, E.; Kumaran, S.; et al. Measurement of brain metabolites in patients with type 2 diabetes and major depression using proton magnetic resonance spectroscopy. *Neuropsychopharmacology* **2007**, *32*(6), 1224-1231. doi:10.1038/sj.npp.1301248
37. Rosenberg, D.R.; Macmaster, F.P.; Mirza, Y.; et al. Reduced anterior cingulate glutamate in pediatric major depression: A magnetic resonance spectroscopy study. *Biol. Psychiatry* **2005**, *58*(9), 700-704. doi:10.1016/j.biopsych.2005.05.007
38. Michael, N.; Erfurth, A.; Ohrmann, P.; Arolt, V.; Heindel, W.; Pfleiderer, B. Neurotrophic effects of electroconvulsive therapy: A proton magnetic resonance study of the left amygdalar region in patients with treatment-resistant depression. *Neuropsychopharmacology* **2003**, *28*(4), 720-725. doi:10.1038/sj.npp.1300085
39. Michael, N.; Erfurth, A.; Ohrmann, P.; Arolt, V.; Heindel, W.; Pfleiderer, B. Metabolic changes within the left dorsolateral prefrontal cortex occurring with electroconvulsive therapy in patients with treatment-

- resistant unipolar depression. *Psychol. Med.* **2003**, 33(7), 1277-1284. doi:10.1017/s0033291703007931
40. Friedman, K.E.; Ashmore, J.A.; Applegate, K.L. Recent experiences of weight-based stigmatization in a weight loss surgery population: Psychological and behavioral correlates. *Obesity (Silver Spring)* **2008**, 16(Suppl 2), S69-S74. doi:10.1038/oby.2008.457
41. Sarwer, D.B.; Fabricatore, A.N.; Eisenberg, M.H.; Sywulak, L.A.; Wadden, T.A. Correction to: Self-reported stigmatization among candidates for bariatric surgery. *Obesity (Silver Spring)* **2010**, 18(4), Art. No: 652. doi:10.1038/oby.2009.484
42. Carpenter, K.M.; Hasin, D.S.; Allison, D.B.; Faith, M.S. Relationships between obesity and DSM-IV major depressive disorder, suicide ideation, and suicide attempts: Results from a general population study. *Am. J. Public Health* **2000**, 90(2), 251-257. doi:10.2105/ajph.90.2.251
43. Guerrini Usubini, A.; Bottacchi, M.; Bondesan, A.; et al. Emotional and behavioral impairment and comorbid eating disorder symptoms in adolescents with obesity: A cross-sectional study. *J. Clin. Med.* **2024**, 13(7), Art. No: 2068. doi:10.3390/jcm13072068
44. Lee, Y.H.; Liu, Z.; Fatori, D.; et al. Association of everyday discrimination with depressive symptoms and suicidal ideation during the COVID-19 pandemic in the All of Us Research Program. *JAMA Psychiatry* **2022**, 79(9), 898-906. doi:10.1001/jamapsychiatry.2022.1973
45. Wang, Y.; Liao, J.; Chen, H.; Tao, L.; Liu, J. Association of perceived discrimination with the risk of depression among US older adults: A prospective population-based cohort study. *Heliyon* **2023**, 10(1), Art. No: e23843. doi:10.1016/j.heliyon.2023.e23843
46. Mahindru, A.; Patil, P.; Agrawal, V. Role of physical activity on mental health and well-being: A review. *Cureus* **2023**, 15(1), e33475. doi:10.7759/cureus.33475
47. WHO guidelines on physical activity and sedentary behaviour: At a glance. Geneva: World Health Organization; **2020**. Licence: CC BY-NC-SA 3.0 IGO.
48. Codella, R.; Chirico, A. Physical Inactivity and Depression: The Gloomy Dual with Rising Costs in a Large-Scale Emergency. *Int. J. Environ. Res. Public Health* **2023**, 20(2), Art. No: 1603. doi:10.3390/ijerph20021603
49. Raiman, L.; Amarnani, R.; Abdur-Rahman, M.; Marshall, A.; Mani-Babu, S. The role of physical activity in obesity: let's actively manage obesity. *Clin. Med. (Lond.)* **2023**, 23(4), 311-317. doi:10.7861/clinmed.2023-0152
50. Carraça, E.V.; Encantado, J.; Battista, F.; et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: A systematic review and meta-analysis. *Obes. Rev.* **2021**, 22(Suppl 4), e13261. doi:10.1111/obr.13261
51. Gualdi-Russo, E.; Rinaldo, N.; Zaccagni, L. Physical Activity and Body Image Perception in Adolescents: A Systematic Review. *Int. J. Environ. Res. Public Health* **2022**, 19(20), 13190. doi:10.3390/ijerph192013190
52. Zaccagni, L.; Gualdi-Russo, E. The Impact of Sports Involvement on Body Image Perception and Ideals: A Systematic Review and Meta-Analysis. *Int. J. Environ. Res. Public Health* **2023**, 20(6), 5228. doi:10.3390/ijerph20065228
53. Singh, B.; Olds, T.; Curtis, R.; et al. Effectiveness of physical activity interventions for improving depression, anxiety and distress: an overview of systematic reviews. *Br. J. Sports Med.* **2023**, 57(18), 1203-1209. doi:10.1136/bjsports-2022-106195
54. Huang, J.H.; Li, R.H.; Tsai, L.C. Relationship between Depression with Physical Activity and Obesity in Older Diabetes Patients: Inflammation as a Mediator. *Nutrients* **2022**, 14(19), 4200. doi:10.3390/nu14194200
55. Pojednic, R.; D'Arpino, E.; Halliday, I.; Bantham, A. The Benefits of Physical Activity for People with Obesity, Independent of Weight Loss: A Systematic Review. *Int. J. Environ. Res. Public Health* **2022**, 19(9), 4981. doi:10.3390/ijerph19094981
56. Xu, P.; Huang, Y.; Hou, Q.; et al. Relationship between physical activity and mental health in a national representative cross-section study: Its variations according to obesity and comorbidity. *J. Affect. Disord.* **2022**, 308, 484-493. doi:10.1016/j.jad.2022.04.037
57. Foley Davelaar, C.M. Body Image and its Role in Physical Activity: A Systematic Review. *Cureus* **2021**, 13(2), e13379. doi:10.7759/cureus.13379
58. Chen, L.; Liu, Q.; Xu, F.; et al. Effect of physical activity on anxiety, depression and obesity index in children and adolescents with obesity: A meta-analysis. *J. Affect. Disord.* **2024**, 354, 275-285. doi:10.1016/j.jad.2024.02.092
59. Pearce, M.; Garcia, L.; Abbas, A.; et al. Association Between Physical Activity and Risk of Depression: A Systematic Review and Meta-analysis. *JAMA Psychiatry* **2022**, 79(6), 550-559. doi:10.1001/jamapsychiatry.2022.0609
60. Curtis, R.G.; Prichard, I.; Gosse, G.; Stankevicius, A.; Maher, C.A. Hashtag fitspiration: credibility screening and content analysis of Instagram fitness accounts. *BMC Public Health* **2023**, 23(1), 421. doi:10.1186/s12889-023-15232-7
61. Jerónimo, F.; Carraça, E.V. Effects of fitspiration content on body image: a systematic review. *Eat. Weight Disord.* **2022**, 27(8), 3017-3035. doi:10.1007/s40519-022-01505-4