REVIEW

The impact of genetics on obesity, metabolic health and healthy weight control: a narrative review

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ABSTRACT

This review article aims to explore the relationship between obesity genes, metabolic health, and the implications for healthy weight control. In the search for scientific literature for this review, data from the US National Library of Medicine (PubMed), MEDLINE, and SportDiscus were used, and the terms "obesity genetics'','' weight control'', ''metabolic health'','' physical activity'',''life quality'', and "obesity" were used. The relevant literature has also taken its source from researching relevant articles from reference lists derived from data searches. Obesity is recognized as a chronic disease characterized by an imbalance between energy intake and expenditure, leading to excessive fat accumulation.

As a result, maintaining metabolic health directly affects healthy aging positively, providing quality life for many years. Healthy aging provides effective defense against chronic conditions while addressing all determinants involving physical components. However, metabolic health; as it can also ensure optimal preservation of mental health functions, ultimately contributes to longevity and high-quality life experiences.

Keywords: Obesity genetics, weight control, physical activity, metabolic health, life quality, obesity

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INTRODUCTION

It is becoming increasingly clear that obesity is a condition that can be influenced by a number of different factors, some of which are environmental and some of which are genetic. While environmental conditions, such as reduced physical activity and irregular energy balance, have long been recognized as significant contributors to obesity, the role of genetic structure has recently emerged as a topic of growing interest. Recent research suggests a potential link between genetic factors and obesity, with particular attention to genes involved in fat metabolism. It is becoming increasingly clear that obesity represents a significant public health concern, affecting millions of people around the globe and contributing to a range of chronic health conditions [1]. It is generally agreed that obesity is defined as an excess accumulation of body fat, and that it results from a complex

interplay between genetic, environmental, and behavioral factors [2].

Obesity is a complex condition influenced by a number of genetic variants that affect fat storage, energy balance, and metabolism. A growing body of literature in this field has identified a number of genes and genetic markers that may be associated with obesity. These include FTO, MC4R, and TMEM18. It seems reasonable to suggest that these genetic factors may predispose individuals to obesity by influencing their metabolic rate, appetite, and fat distribution [3, 4, 5].

There seems to be growing evidence that metabolic health, healthy aging, and well-being are important issues to consider. Metabolic health refers to the body's ability to efficiently process and use energy from food, while healthy aging involves maintaining physical, mental, and social well-being as individuals age. Research has shown that maintaining metabolic health can have a significant impact on overall quality of life and longevity. For example, a study by Zhang (2023) found that individuals who actively maintained their metabolic health experienced higher quality of life and increased longevity compared to those who did not prioritize their metabolic well-being [6]. As the people age, it becomes increasingly important to consider ways to maintain metabolic health, prevent chronic disease, and enhance vitality in later years. This can be achieved through various lifestyle interventions such as regular physical activity, balanced diet, weight control, and stress management. Tavares (2017) emphasizes the holistic nature of healthy aging, highlighting the interconnectedness of physical, mental, and social well-being [7]. Therefore, it may be useful to consider ways to develop effective health strategies that address many different aspects of health and well-being in the elderly, especially issues related to cardiovascular disease and metabolic health. It may be useful to consider metabolic health, life quality and healthy aging from various perspectives in the field of human health, including obesity genetics [8].

Some research suggests that regular physical activity may potentially influence genetic predispositions to obesity. A number of studies have indicated that consistent physical exercise may have the potential to mitigate the influence of obesity-related genes on an individual's BMI. This suggests that physical activity may be a valuable addition to the toolkit of strategies for mitigating genetic risk [9, 10].

The interplay between genetic factors and obesity has significant implications for an individual's quality of life. Obesity is linked to numerous psychosocial issues, including reduced self-esteem and increased risk of mental health disorders. Therefore, understanding and addressing the genetic factors contributing to obesity can improve metabolic health and enhance the overall quality of life [11, 12].

It would seem that gender-specific responses to physical activity may also be a significant factor in understanding the genetic predisposition to obesity. It seems that men may derive greater benefits from regular physical activity in mitigating the genetic risk for obesity compared to women. This difference highlights the need to demonstrate the potential value of considering gender-specific recommendations and interventions in

the prevention and management of obesity [13, 14, 15].

DISCUSSION

It seems that obesity is a multifactorial disease, influenced by a number of different factors, including environmental and genetic factors [16]. While lifestyle choices and environmental conditions undoubtedly play a significant role, there is mounting evidence to suggest that genetic structure may also be a crucial component in understanding obesity etiology [17]. Recent advances in genomic research have led to the identification of a number of genetic variants that appear to be associated with an increased risk of obesity [18].

It is becoming increasingly clear that obesity is not just a cosmetic problem. There is growing evidence that it is a significant precursor to many chronic health issues that can have a severe impact on an individual's quality of life and longevity. Research has consistently demonstrated a potential correlation between obesity and various conditions, including type 2 diabetes mellitus, which is characterized by insulin resistance and often leads to serious complications such as neuropathy and retinopathy [19]. Furthermore, it is worth noting that obesity may be a contributing factor to cardiovascular disease (CVD). Excess body fat can potentially lead to hypertension, dyslipidemia, and increased arterial stiffness, which may in turn contribute to the development of atherosclerosis and heart attacks.

In addition to metabolic disorders, there is also a link between obesity and metabolic syndrome, which is a cluster of conditions that can increase the risk of heart disease, stroke, and diabetes. This syndrome is characterized by a number of factors, including abdominal obesity, elevated blood pressure, high blood sugar levels, and abnormal cholesterol levels. It is also thought that certain cancers, such as breast, colorectal, and endometrial cancers, may be linked to obesity. This is because excess adipose tissue may alter hormone levels and inflammatory pathways, creating an environment conducive to tumor growth [20, 21].

Furthermore, it is important to consider the psychological effects of obesity. Individuals with obesity may face stigma and discrimination, which can contribute to mental health issues such as depression and anxiety. These psychological conditions can further impact overall health, creating a challenging cycle where emotional distress may lead to further weight gain and health deterioration [22]. Therefore, addressing obesity requires a comprehensive approach that considers both physical and mental health aspects.

The causes of obesity are complex and not fully understood. It seems that there is an imbalance in energy homeostasis, whereby the amount of calories consumed exceeds the amount of energy expended [23]. It is thought that this imbalance may have its roots in dietary habits, physical inactivity, and genetic predispositions. It is also worth noting that the body's ability to regulate energy expenditure is influenced by various organs and systems, including the endocrine and nervous systems. When these systems are unable to function as they should, excess energy is stored in adipose tissue, primarily as triglycerides, which can lead to overweight and obesity [24, 25].

Recent studies have indicated that genetic factors may play a role in determining an individual's susceptibility to obesity. It seems that these genetic predispositions can interact with various lifestyle factors, such as diet and physical activity, which may ultimately influence the risk of developing obesity. As our understanding of the genetic basis of obesity continues to evolve, there is a growing interest in exploring the potential of advanced genetic analysis techniques to identify specific genetic markers associated with obesity [26]. One area that has recently come to the fore in obesity research is the potential interaction between genetic factors and physical activity levels. A number of studies have explored the possibility that regular physical activity may influence the impact of obesity-related genetic variants [27]. Based on all these research results, by incorporating lifestyle, diet, etc. into personalized interventions, it is thought that healthcare professionals will be able to tailor obesity prevention and treatment strategies to better suit individual needs. This personalized approach may be a promising way to develop more effective and targeted interventions aimed at reducing the prevalence of obesity and improving overall public health that may highlight the potential for obesity risk [28].

It would seem that there is a growing body of evidence to suggest that obesity may have a heritable component, with estimates of heritability ranging from 40% to 70% [29]. It is worth noting that genome-wide association studies (GWAS) have identified over 900 genetic loci associated with obesity-related traits, which seems to indicate that obesity susceptibility may be polygenic in nature [30, 31].

A study by Li et al. (2010) explored the potential interaction between the FTO gene, which is associated with obesity risk, and physical activity [13]. The study indicated that the correlation between FTO variants and obesity risk appeared to be reduced in physically active individuals compared to less active individuals. This finding suggests that regular physical activity may have the potential to reduce genetic predisposition to obesity.

Similarly, a study by Kilpeläinen et al. (2011) found evidence that the effects of obesity-predisposing alleles may be reduced in physically active individuals [32]. The study is important in showing that there may be a difference in the effect of each additional risk allele on BMI depending on the level of physical activity, and that regular exercise may have positive health effects on obesity and overweight that may develop due to obesity-predisposing alleles.

Some studies have indicated the possibility of gender-specific differences in the interaction between genetic factors and physical activity in relation to obesity. Ahmad et al. (2013) observed that the attenuation of the genetic predisposition to obesity through physical activity appeared to be more pronounced in men compared to women [33]. However, the authors suggested that this finding should be further investigated and replicated in diverse populations.

As the knowledge of gene-environment interactions in the development of obesity continues to evolve, it is becoming increasingly clear that this has significant implications for the prevention and treatment of this complex condition. While genetic factors may play a role in an individual's susceptibility to obesity,

the modifying effect of physical activity suggests that lifestyle interventions may still be important in obesity management [34]. It may be beneficial to consider personalized approaches that take into account an individual's genetic profile and tailor physical activity recommendations accordingly, with the aim of potentially increasing the effectiveness of obesity prevention and treatment programs [35]. Nevertheless, further research would undoubtedly be beneficial in order to facilitate the translation of these findings into clinical practice.

CONCLUSION

Obesity is a chronic disease caused by an imbalance between energy intake and expenditure, resulting in the accumulation of fat in the body. This imbalance can be attributed to both excessive calorie intake and inadequate energy expenditure by the body's organs and systems. The inefficient utilization of food intake leads to the storage of fatty acids in adipose tissue, contributing to overweight and obesity. Obesity is a serious health problem that can lead to various metabolic issues, such as type 2 diabetes, depression, musculoskeletal problems, metabolic syndrome, cancer, fatty liver, hormonal disorders, hypertension, and cardiovascular disease. The progression of obesity may vary from person to person, and factors like age and gender can influence it. Studies have shown that men tend to store less fat compared to women with the same Body Mass Index. Obesity is not only influenced by age and gender but also by a range of metabolic factors. Genetic factors also play a significant role in regulating metabolic processes and controlling energy storage and expenditure.

The rising rates of obesity globally indicate the urgent need for prevention and treatment strategies. While environmental factors contribute to obesity, genetics also play a significant role. Research suggests a correlation between genetics and physical activity, with regular exercise potentially reducing the hereditary effects of obesity-causing genes on Body Mass Index (BMI). Studies show that exercising for at least 45 minutes a day, five days a week, can mitigate the genetic influence on BMI. However, this effect may be more pronounced in men compared to women. These findings highlight the importance of regular physical activity in preventing obesity, particularly in individuals with a genetic predisposition. Further research in this area is needed to develop effective strategies for addressing this global public health issue.

Research studies suggest that there may be a complex interplay between genetic factors, physical activity, and obesity risk. While genetic predisposition undoubtedly plays an important role in the development of obesity, evidence suggests that regular physical activity may help to reduce the effects of genetic variants associated with obesity. These findings highlight the potential value of promoting physical activity as a key element in obesity prevention and treatment strategies, even among individuals with a genetic predisposition to obesity.

While the positive interaction between the genetic structure that can cause overweight and obesity and regular physical activity can provide valuable insights, it is evident that further research in this area is necessary to gain a more comprehensive understanding. It is becoming increasingly clear that obesity can

have a significant impact on an individual's quality of life, and that this can in turn give rise to a number of psychosocial issues. It is therefore hoped that the development and dissemination of genetic analysis methods in the prevention and treatment of obesity, which is considered a global health problem, will make a positive contribution to the solution of the overweight and obesity problem.

It would be beneficial for future research to focus on clarifying the molecular mechanisms underlying the interaction between genetics and physical activity in obesity, as well as investigating potential sex-specific effects. Furthermore, it would be beneficial to conduct long-term intervention studies to ascertain the most effective type, intensity, and duration of physical activity for reducing the risk of genetic obesity in diverse populations.

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REFERENCES

1. World Health Organization (2023). Obesity and overweight. Retrieved from https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

2. Kahn SE, Cooper ME, Del Prato S. Pathophysiology and treatment of type 2 diabetes: perspectives on the past, present, and future. Lancet. 2014 Mar 22;383(9922):1068-83.

3. Berseneva A, Kovalenko E, Vergasova E, et al. Association of common genetic variants with body mass index in Russian population. Eur J Clin Nutr. 2023 May;77(5):574-578.

4. Lim U, Le Marchand L, Wilkens L. Genetic studies of body mass index yield new insights for obesity biology. 2015.

5. Locke AE, Kahali B, Berndt SI, et al. Genetic studies of body mass index yield new insights for obesity biology. Nature. 2015 Feb 12;518(7538):197-206.

6. Zhang K, Ma Y, Luo Y, Song Y, Xiong G, Ma Y, Sun X, Kan C. Metabolic diseases and healthy aging: identifying environmental and behavioral risk factors and promoting public health. Front Public Health. 2023 Oct 13;11:1253506.

7. Tavares RE, Jesus MCPD, Machado DR, Braga VAS, Tocantins FR, Merighi MAB. Healthy aging from the perspective of the elderly: an integrative review. Revista brasileira de geriatria e gerontologia, 2017;20, 878-889.

8. Sanghera DK, Bejar C, Sharma S, Gupta R, Blackett PR. Obesity genetics and cardiometabolic health: Potential for risk prediction. Diabetes Obes Metab. 2019 May;21(5):1088-1100.

9. Herring MP, Sailors MH, Bray MS. Genetic factors in exercise adoption, adherence and obesity. Obes Rev. 2014 Jan;15(1):29-39.

10. Switala K, Leonska-Duniec A. Physical activity and gene association with human obesity. Baltic Journal of Health and Physical Activity, 2021;13(4), 10.

11. Lin X, Li H. Obesity: Epidemiology, Pathophysiology, and Therapeutics. Front Endocrinol (Lausanne). 2021 Sep 6;12:706978.

12. Taylor VH, Forhan M, Vigod SN, McIntyre RS, Morrison KM. The impact of obesity on quality of life. Best Pract Res Clin Endocrinol Metab. 2013 Apr;27(2):139-46.

13. Li S, Zhao JH, Luan J, Ekelund U, Luben RN, Khaw KT, Wareham NJ, Loos RJ. Physical activity attenuates the genetic predisposition to obesity in 20,000 men and women from EPIC-Norfolk prospective population study. PLoS Med. 2010 Aug 31;7(8):e1000332.

14. Lin WY, Chan CC, Liu YL, Yang AC, Tsai SJ, Kuo PH. Performing different kinds of physical exercise differentially attenuates the genetic effects on obesity measures: Evidence from 18,424 Taiwan Biobank participants. PLoS Genet. 2019 Aug 1;15(8):e1008277.

15. Williams PT. Attenuating effect of vigorous physical activity on the risk for inherited obesity: a study of 47,691 runners. PLoS One. 2012;7(2):e31436.

16. Hruby A, Hu FB. The Epidemiology of Obesity: A Big Picture. Pharmacoeconomics. 2015 Jul;33(7):673-89.

17. Loos RJF, Yeo GSH. The genetics of obesity: from discovery to biology. Nat Rev Genet. 2022 Feb;23(2):120-133.

18. Goodarzi MO. Genetics of obesity: what genetic association studies have taught us about the biology of obesity and its complications. Lancet Diabetes Endocrinol. 2018 Mar;6(3):223-236.

19. Huang JX, Liao YF, Li YM. Clinical Features and Microvascular Complications Risk Factors of Early-onset Type 2 Diabetes Mellitus. Curr Med Sci. 2019 Oct;39(5):754-758.

20. Cai L, He J, Song Y, Zhao K, Cui W. Association of obesity with socio-economic factors and obesity-related chronic diseases in rural southwest China. Public Health. 2013 Mar;127(3):247-51.

21. Rippe JM, Crossley S, Ringer R. Obesity as a chronic disease: modern medical and lifestyle management. J Am Diet Assoc. 1998 Oct;98(10 Suppl 2):S9-15.

22. Atlantis E, Baker M. Obesity effects on depression: systematic review of epidemiological studies. Int J Obes (Lond). 2008 Jun;32(6):881-91.

23. Webber J. Energy balance in obesity. Proc Nutr Soc. 2003 May;62(2):539-43.

24. Frühbeck G. Overview of adipose tissue and its role in obesity and metabolic disorders. Methods Mol Biol. 2008;456:1-22.

25. van de Woestijne AP, Monajemi H, Kalkhoven E, Visseren FL. Adipose tissue dysfunction and hypertriglyceridemia: mechanisms and management. Obes Rev. 2011 Oct;12(10):829-40.

26. Tam V, Turcotte M, Meyre D. Established and emerging strategies to crack the genetic code of obesity. Obes Rev. 2019 Feb;20(2):212-240.

27. Reddon H, Gerstein HC, Engert JC, et al. Physical activity and genetic predisposition to obesity in a multiethnic longitudinal study. Sci Rep. 2016 Jan 4;6:18672.

28. Popp CJ, Hu L, Kharmats AY, et al. Effect of a Personalized Diet to Reduce Postprandial Glycemic Response vs a Low-fat Diet on Weight Loss in Adults With Abnormal Glucose Metabolism and Obesity: A Randomized Clinical Trial. JAMA Netw Open. 2022 Sep 1;5(9):e2233760.

29. Elks CE, den Hoed M, Zhao JH, et al. Variability in the heritability of body mass index: a systematic review and meta-regression. Front Endocrinol (Lausanne). 2012 Feb 28;3:29.

30. Concepción-Zavaleta MJ, Quiroz-Aldave JE, Durand-Vásquez MDC, et al. A comprehensive review of genetic causes of obesity. World J Pediatr. 2024 Jan;20(1):26-39.

31. Yengo L, Sidorenko J, Kemper KE, et al; GIANT Consortium. Meta-analysis of genome-wide association studies for height and body mass index in ~700000 individuals of European ancestry. Hum Mol Genet. 2018 Oct 15;27(20):3641-3649.

32. Kilpeläinen TO, Qi L, Brage S, et al. Physical activity attenuates the influence of FTO variants on obesity risk: a meta-analysis of 218,166 adults and 19,268 children. PLoS Med. 2011 Nov;8(11):e1001116.

33. Ahmad S, Rukh G, Varga TV, et al. Gene × physical activity interactions in obesity: combined analysis of 111,421 individuals of European ancestry. PLoS Genet. 2013;9(7):e1003607.

34. Hebebrand J, Hinney A, Knoll N, Volckmar AL, Scherag A. Molecular genetic aspects of weight regulation. Dtsch Arztebl Int. 2013 May;110(19):338-44. doi: 10.3238/arztebl.2013.0338. Epub 2013 May 10.

35. Ramos-Lopez O, Milagro FI, Allayee H, et al. Guide for Current Nutrigenetic, Nutrigenomic, and Nutriepigenetic Approaches for Precision Nutrition Involving the Prevention and Management of Chronic Diseases Associated with Obesity. J Nutrigenet Nutrigenomics. 2017;10(1-2):43-62.

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