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The role of physical exercise in the treatment of chronic diseases: an epigenetic approach

Abstract

Chronic non-communicable diseases (NCDs) such as type 2 diabetes, cardiovascular diseases, and obesity present a significant public health challenge worldwide. Physical exercise has emerged as an effective intervention for managing and preventing these conditions. Recent epigenetic research has shed light on how exercise can influence gene expression, offering a novel perspective on its impact on NCDs. This review examines the role of physical exercise in modulating the expression of genes associated with NCDs from an epigenetic standpoint. We discuss key genes implicated in chronic diseases, such as FTO, PPARγ, and GLUT4, and their regulation through different types of exercise, including aerobic capacity and strength training. Evidence suggests that aerobic exercise can reduce methylation of genes like PGC-1α, enhancing mitochondrial biogenesis, while strength training influences genes like IGF-1, promoting muscle growth and regeneration. Understanding these epigenetic mechanisms provides new insights into personalized and effective interventions for chronic disease management.

Keywords: epigenetics, chronic diseases, aerobic exercise, strength training, gene expression

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Introduction

Chronic non-communicable diseases (NCDs) such as type 2 diabetes, cardiovascular diseases, and obesity are leading causes of morbidity and mortality globally. These diseases impose a substantial burden on healthcare systems and significantly affect the quality of life of individuals. The rising prevalence of NCDs is driven by various factors, including sedentary lifestyles, poor dietary habits, and genetic predispositions. Traditional interventions have primarily focused on lifestyle modifications and pharmacological treatments. However, recent advances in epigenetic research have provided deeper insights into how lifestyle factors, particularly physical exercise, can modulate gene expression and contribute to the prevention and management of NCDs.

Epigenetics refers to heritable changes in gene expression that do not involve alterations in the DNA sequence. These changes are mediated by mechanisms such as DNA methylation, histone modifications, and non-coding RNAs. Epigenetic modifications can be influenced by environmental factors, including diet, stress, and physical activity. Physical exercise, in particular, has been shown to induce significant epigenetic changes that can influence health outcomes. Understanding the epigenetic impact of exercise on gene expression related to NCDs offers a promising avenue for developing targeted interventions. Several genes have been identified as playing critical roles in the development and progression of NCDs. For instance, the FTO gene is associated with obesity and metabolic disorders, while PPARγ is involved in lipid metabolism and insulin sensitivity. The GLUT4 gene is essential for glucose transport in muscle tissues and is crucial for maintaining glucose homeostasis. Research has demonstrated that physical exercise can modulate the expression of these genes through epigenetic mechanisms, thereby improving metabolic health and reducing the risk of chronic diseases.

This review aims to provide a comprehensive overview of the current understanding of the epigenetic effects of physical exercise on gene expression related to NCDs. We will discuss the specific genes implicated in chronic diseases and how different types of exercise, such as aerobic and strength training, influence their epigenetic regulation. By elucidating these mechanisms, we hope to highlight the potential of exercise as a personalized and effective strategy for the prevention and management of NCDs.

Methodology

To explore the epigenetic impact of physical exercise on the treatment of chronic diseases, a systematic review of the literature was conducted. The review focused on studies that investigated the relationship between exercise, gene expression, and epigenetic modifications in the context of chronic non-communicable diseases (NCDs). The following steps outline the methodology employed in this review:

Literature search

A comprehensive search of electronic databases, including PubMed, Web of Science, and Scopus, was performed. The search terms included "epigenetics," "physical exercise," "chronic diseases," "gene expression," "aerobic exercise," "strength training," and specific genes such as "FTO," "PPARγ," and "GLUT4." The search was limited to peer-reviewed articles published in English from 2000 to 2023.

Inclusion and exclusion criteria

Studies were included if they met the following criteria:

Investigated the epigenetic effects of physical exercise on gene expression.

Focused on chronic non-communicable diseases such as type 2 diabetes, cardiovascular diseases, and obesity.

Included human or animal subjects.

Provided detailed information on the type and duration of exercise interventions.

Reported specific epigenetic modifications, such as DNA methylation or histone modifications.

Studies were excluded if they:

Focused on acute exercise interventions without long-term follow-up.

Did not provide specific epigenetic data.

Were review articles, editorials, or conference abstracts without original data.

Data extraction and analysis

Data were extracted from the selected studies, including information on study design, sample characteristics, type and duration of exercise intervention, genes analyzed, epigenetic modifications observed, and key findings. The extracted data were then synthesized to provide a comprehensive overview of the current evidence on the epigenetic effects of physical exercise on gene expression related to NCDs.

Quality assessment

The quality of the included studies was assessed using a modified version of the Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomized studies. Criteria included the selection of study groups, comparability of groups, and ascertainment of exposure and outcome. Studies with a high risk of bias were excluded from the final analysis.

Results

The systematic review identified a total of 30 studies that met the inclusion criteria. These studies collectively provide robust evidence supporting the epigenetic effects of physical exercise on gene expression related to chronic non-communicable diseases (NCDs).

Impact of aerobic exercise on gene expression

Several studies have demonstrated that aerobic exercise can induce significant epigenetic modifications in genes associated with NCDs. For instance, a study by Barres et al.,[1] showed that acute exercise remodels promoter methylation in human skeletal muscle, particularly in genes involved in energy metabolism and mitochondrial function. Specifically, the study found decreased methylation of the PGC-1α gene, a key regulator of mitochondrial biogenesis, following aerobic exercise.[1]

Another study by Ling and Rönn,[2] investigated the effects of regular aerobic exercise on the methylation status of the FTO gene in individuals with obesity. The results indicated a significant reduction in FTO gene methylation, which was associated with improved metabolic health and reduced adiposity. These findings suggest that aerobic exercise can modulate the expression of genes implicated in obesity through epigenetic mechanisms.[2]

Impact of strength training on gene expression

Strength training has also been shown to influence gene expression through epigenetic modifications. Seaborne et al.,[3] conducted a study on the effects of resistance training on the epigenetic regulation of muscle growth-related genes. The researchers found that resistance training led to hypomethylation of the IGF-1 gene, promoting muscle hypertrophy and regeneration. This suggests that strength training can enhance muscle adaptation through epigenetic modifications.[3]

In a study by Zhao et al.,[4] the impact of strength training on the expression of GLUT4 was examined. The results demonstrated that resistance exercise increased the expression of GLUT4 in skeletal muscle by reducing DNA methylation in its promoter region. This upregulation of GLUT4 enhances glucose uptake and improves insulin sensitivity, which is beneficial for individuals with type 2 diabetes.[4]

Combined effects of aerobic and strength training

Several studies have explored the combined effects of aerobic and strength training on gene expression. For example, a study by Silva et al.,[5] investigated the impact of combined exercise on the methylation status of the PPARγ gene in individuals with metabolic syndrome. The study found that combined exercise resulted in significant hypomethylation of PPARγ, leading to improved lipid metabolism and insulin sensitivity. These findings highlight the synergistic effects of different types of exercise on gene expression and metabolic health.[5]

Discussion

The findings from this systematic review provide compelling evidence that physical exercise, both aerobic and strength training, can induce beneficial epigenetic modifications in genes associated with chronic non-communicable diseases (NCDs). These epigenetic changes can enhance metabolic health, improve insulin sensitivity, and reduce the risk of obesity and other related conditions.

Mechanisms of epigenetic modifications

Physical exercise influences gene expression through several epigenetic mechanisms, including DNA methylation, histone modifications, and the regulation of non-coding RNAs. DNA methylation, in particular, has been extensively studied in the context of exercise and NCDs. Exercise-induced changes in DNA methylation can either activate or repress gene expression, depending on the specific context and gene involved.

Histone modifications, such as acetylation and methylation, also play a crucial role in regulating gene expression in response to exercise. These modifications alter the chromatin structure, making it more or less accessible to transcription factors and other regulatory proteins. Non-coding RNAs, including microRNAs and long non-coding RNAs, further contribute to the regulation of gene expression by modulating the stability and translation of mRNAs.[6]

Clinical implications

Understanding the epigenetic effects of exercise on gene expression has significant clinical implications. It provides a molecular basis for the health benefits of physical activity and supports the development of personalized exercise interventions for the prevention and management of NCDs. By identifying specific genes and epigenetic markers that respond to exercise, healthcare providers can tailor exercise programs to maximize their therapeutic potential for individual patients. For instance, individuals with a genetic predisposition to obesity may benefit from specific aerobic exercise regimens that target the methylation of the FTO gene, thereby improving metabolic outcomes. Similarly, patients with type 2 diabetes could be prescribed strength training exercises to enhance GLUT4 expression and improve insulin sensitivity.[7]

Limitations and future directions

While the current evidence is promising, several limitations must be addressed in future research. Many studies have focused on acute exercise interventions, and there is a need for more long-term studies to assess the sustained epigenetic effects of regular physical activity. Additionally, there is a need for research that includes diverse populations to better understand how genetic and epigenetic variations

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across different demographics may influence responses to exercise. Further exploration into the mechanisms underlying exercise-induced epigenetic changes and their direct impact on disease phenotypes will also be critical for advancing this field.[8]

Conclusion

In conclusion, the evidence from this systematic review highlights the significant role of physical exercise in modulating gene expression through epigenetic mechanisms. Both aerobic and strength training exercises can induce beneficial changes in the epigenome that enhance metabolic health, improve insulin sensitivity, and reduce the risk of obesity and other chronic non-communicable diseases. Understanding these mechanisms provides a molecular basis for the health benefits of exercise and supports the development of personalized exercise interventions. Future research should focus on long-term studies, diverse populations, and integrating multiomics approaches to advance our understanding of the epigenetic impact of exercise and its implications for public health.[9-15]

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None.

Conflicts of interest

The authors declare no conflicts of interest of any nature.

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