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The influence of mindfulness exercises on epigenetic regulation in inflammatory genes

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ABSTRACT

OBJECTIVE

To analyze the relationship between mindfulness, epigenetics, and inflammation, investigating its effects on DNA methylation regulation and inflammatory genes.

METHOD

A systematic review was conducted following the PRISMA guidelines, with searches in PubMed (2013-2023), including clinical trials and observational studies that addressed the interaction between mindfulness and DNA methylation in inflammatory genes, excluding animal models and small samples.

RESULTS

It was observed that mindfulness practice reduces the expression of pro-inflammatory genes, modulates epigenetic pathways, and contributes to the improvement of mental and cardiovascular health, positively impacting cellular longevity. Conclusion: It is concluded that mindfulness can be an effective strategy for manipulating inflammatory processes and gene expression. However, further research is urgently needed to confirm its applicability in different populations.

CONCLUSION

It is concluded that mindfulness can be an effective strategy for manipulating inflammatory processes and gene expression. However, further research is urgently needed to confirm its applicability in different populations.

KEYWORDS

Mindfulness; DNA methylation; Epigenetics.

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INTRODUCTION

Mindfulness meditation is a set of practices aimed at developing present-moment attention, without judgment, through the exploration of present-moment-based conscious mental states and applied attention. From a historical perspective, this theoretical methodology was created by the American researcher Jon Kabat-Zinn, who gathered important aspects of Eastern culture, mainly based on Buddhist spiritualism, and adapted them into a version more palatable to Western culture. Amidst the recorded clinical impacts, this approach spread worldwide from the 1970s onwards and has studies proving its applications in various medical and other health fields.[1]

From this perspective, it is observed that one of the main factors responsible for altering human methylation patterns, and subsequently mimicking the emergence of chronic inflammatory diseases, is social stress. It is the triggering stimulus for the recruitment of numerous inflammation factors, which disperse to various tissues of the human body and generate a long-term potential for tissue lysis, or consequently, increase susceptibility to the development of these chronic diseases.[2-8] Stress is also responsible for stimulating the emergence of various immersive relaxation practices, such as the meditation line explored throughout this article.[1]

In this scenario, the emergence of chronic pathologies after a major negative psychological impact event in the patient's life, such as the diagnosis of metabolic diseases, neurological disorders, immune system dysfunction, cancer, or heart conditions, becomes common.[8] In contrast, meditation practices primarily aim to achieve inverse results to the aforementioned situations, at an epigenetic level. That is, by deactivating the brain's default mode network (DMN) stress areas, individuals are able to decrease hormonal levels linked to hyperactivity, such as cholesterol and noradrenaline, with emphasis on the latter substance, which plays a dual role as a neurotransmitter and a hormone responsible for maintaining chronic stress. [5]

Thus, one of the main representatives of the inflammatory lineage is the group of carotid arterial diseases. These are responsible for a vast number of deaths worldwide, affecting, for example, one of the greatest global powers today, the United States, which suffers an annual economic deficit of 444 billion dollars due to the significant number of related deaths.[4]

Furthermore, the emergence of coronary heart disease (CHD) is intimately linked to the increase in pro-inflammatory cytokines, mainly interleukin 6 (IL-6) and tumor necrosis factor α (TNF-α). However, in this specific case, such compounds are responsible for causing endothelial cell dysfunction by inhibiting nitric oxide synthesis, a substance that performs various functions for maintaining the homeostasis of vascular structures.[4]

In contrast, the objective of the mindfulness method is precisely to reverse this generalized state of stress, through daily 30-minute sessions over approximately 3 years, since the observed epigenetic effects are consistent with the durability of the process. Therefore, generally speaking, it is plausible to state that the longer the practice time, the more relevant the effects obtained and, consequently, the greater the positive impact on the patient's life.[2]

Moreover, it is essential to emphasize the benefits promoted by mindfulness related to the mental health of its practitioners. The state of fullness is responsible for reducing inflammation levels in the body, and its origin stems from the production of a special substance, brain-derived neurotrophic factor (BDNF). This factor modulates an individual's post-stress response, and in parallel, its methylation is closely associated with states of mental disorder manifested by psychiatric patients, such as depression, anxiety, and post-traumatic stress, which further highlights the versatility that this treatment can offer.[9]

Thus, mindfulness is defined as a methodology based on disconnecting from the surrounding environment, where practitioners will show significant reductions in chronic stress levels developed by daily activities. In this sense, some systemic findings characteristic of this meditative practice include decreased levels of cholesterol, blood pressure, heart rate, and triglycerides.[1]

In addition, other more specific results for the topic were found, such as: decreased expression of pro-inflammatory genes of the HDAC2, HDAC3, HDAC9, RIPK2, and COX2 lineages,[2,10] consistent attenuation of serum levels of IL-6 and TNF-α, caused by a downregulation process of the NF-κß inflammatory pathway.[3] Furthermore, the presence of 61 differentially methylated sites was evidenced in mindfulness practitioners compared to a group that does not use such practice, in genes determining the immune system and aging.[11] That is, the results suggest that the alteration of these specific nitrogenous base clusters will be capable of modifying an individual's epigenetic profile, through differentiated transcriptional pattern manifestation and, consequently, modified gene expression.[3]

In summary, the study describes the relationship between mindfulness, epigenetics, and inflammation, observing its effects on the regulation of DNA methylation and inflammatory genes, and demonstrating modifications in the expression of human inflammatory biomarkers. The objective is to expand scientific research and the development of therapeutic interventions for modulating gene expression, with a focus on organismal senescence. Additionally, it was investigated how epigenetic alterations promoted by mindfulness practices positively influence inflammatory processes, contributing to the improvement of physical and mental health, as a complementary therapeutic approach in different contexts.

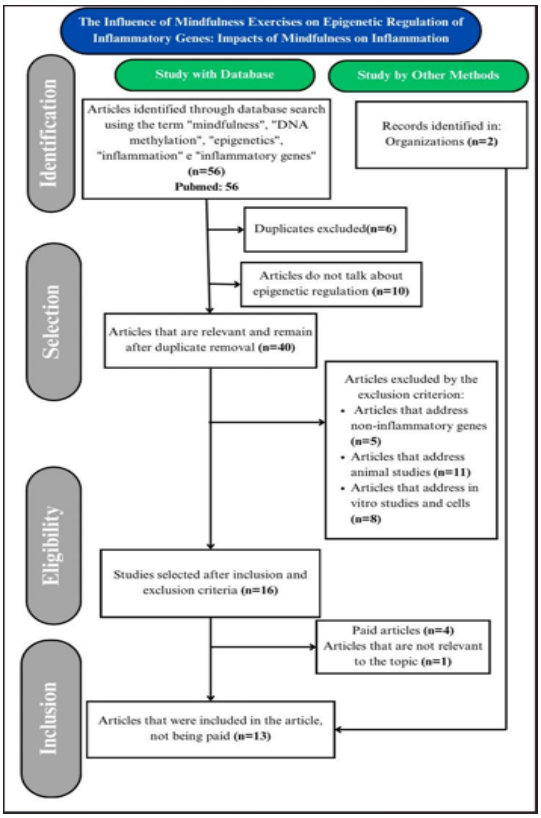
METHODS

This is a systematic literature review, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The research was conducted based on the following guiding question: "What are the effects of mindfulness exercises on DNA methylation patterns in inflammatory genes in adults, according to evidence from clinical and observational studies?" To structure the research strategy, the PICO model was used: P (population) – adults exposed to stress or inflammatory conditions; I (intervention) – mindfulness-based practices; C (comparator) – absence of intervention or non-mindfulness-based therapies; O (outcome) – epigenetic changes, especially in the methylation of pro-inflammatory genes.

From this structure, the selection of descriptors, eligibility criteria, and analysis of included studies were defined. The search was conducted in the PubMed, Scopus, Web of Science, and Embase databases, considering studies published between 2013 and 2023. MeSH (Medical Subject Headings) descriptors such as "mindfulness", "DNA methylation", "epigenetics", "inflammation", and "inflammatory genes" were used, with adjustments according to the syntax of each database, using Boolean operators (AND and OR) to refine the results. Inclusion criteria encompassed studies conducted in humans (≥ 18 years), original articles (clinical trials, cohort, and cross-sectional studies) that analyzed the relationship between mindfulness practices and DNA methylation in inflammatory genes (e.g., TNF-α, IL-6, and CRP), published in English or Portuguese. Studies conducted on animal models, review articles, small samples (n < 20), or with insufficient methodological data were excluded.

The retrieved articles were processed in Rayyan software for duplicate removal and screened by two independent reviewers, with conflict resolution by a third reviewer if necessary. Data collection included information such as participant characteristics, details of mindfulness interventions (type, duration, frequency), methods used for methylation pattern analysis, and results on epigenetic changes in inflammatory genes after practice. The methodological quality of the studies was assessed using the Joanna Briggs Institute Critical Appraisal Checklist,[12] and the level of evidence was classified based on the Oxford Centre for Evidence-Based Medicine scale.[13] The collected data were analyzed to identify methylation patterns in genes related to the inflammatory response from mindfulness practices, emphasizing potential health benefits.

Figure 1 - Prisma Flowchart



Source: Authors (2025)

RESULTS

The results are expressed in Table 1.

Table 1 - Studies on the effects of mindfulness on the methylation of inflammatory genes

STUDY	INTERVENTION	POPULATION	BIOMARKES EVALUATED	DETAILED FINDINGS
Sanada et al.,[1] 2020	Mindfulness (p-value: 0.043)	998 psychiatric patients (depression, generalized anxiety, ADHD, and alcohol dependence)	IL-6, TNF-α, ACTH	Reduction of IL-6 and TNF-α and improvement in ACTH levels.
Kripalani et al.,[2] 2022	Mind-body therapies (yoga, mindfulness meditation, and tai-chi-chuan) (no p-value)	500 women practicing tai-chi--chuan, 28 women with psychological stress practicing yoga, and 40 individuals practicing mindfulness	Genes associated with inflammation, stress response, and aging	Reduced methylation in the TNF gene, indicating potential anti-inflammat ory effects, regulation of stress epigenetics, and deceleration of the epigenetic clock.
Álvarez-López et al.,[3] 2022	1-month meditation retreat (p-value: 0.007)	62 individuals (28 experienced meditators and 34 experienced practitioners)	TNF-α, epigenetic genes, and expression of inflammatory markers	Reduction in TNF-α expression and its receptors, indicating less inflammation and regulation of epigenetic genes, suggesting effects on inflammatory response modulation.
Kaliman et al.,[7] 2022	Multimodal program (mindfulness, artistic expression, and PTSD therapy - Post-Traumatic Stress Disorder) (p-value < 0.001)	44 adolescent females with a history of adverse childhood experiences	Genes related to inflammation, neurodevelop ment, stress response, cancer, and cardiovascular diseases	Epigenetic alterations in genes associated with modulation of inflammatory response, neuroplasticity, and cellular aging. Improvement in PTSD symptoms.
Chaix et al.,[11] 2020	Intensive day of mindfulness meditation (8 hours) (p-Value < 0.05)	34 individuals (17 experienced meditators and 17 controls with no prior meditation experience)	DNA methylation, genes associated with inflammation, immune metabolism, cellular aging, and stress response	Significant increase in methylation of genes associated with inflammatory modulation and immune function.
Lin et al.,[5] 2021	Relaxation response induced by meditation and musical appreciation (p-value < 0.05)	120 individuals (90 post-acute myocardial infarction patients and 30 healthy controls)	Circulating MicroRNAs, telomerase activity, and salivary cortisol	Increase in telomerase and alterations in miRNAs related to inflammation and immunological regulation. Reduction in salivary cortisol, indicating lower stress response.
Aguilar-Raab et al.,[6] 2018	Cognitively Based Compassion Training (CBCT), which cultivates compassion and emotional well--being (No p-value)	Heterosexual couples with female partner diagnosed with mild to moderate depressive disorder	Cortisol, pro-inflammatory cytokines, heart rate variability, methylation of OXTR (oxytocin receptor) and SLC6A4 (serotonin transporter) genes	Reduction of depressive symptoms in the female partner, improvement of couple's social interaction, and modulation of stress biomarkers (decrease in cortisol and changes in methylation of emotional regulation genes).

Legend: ADHD: Attention Deficit Hyperactivity Disorder; ACTH: adrenocorticotropic hormone.

Source: Authors (2025)

The results presented in this systematic review strongly demonstrate that mindfulness-based practices positively influence epigenetic mechanisms and inflammatory processes, offering potential benefits in diverse areas such as mental health, physical well-being, and cognitive performance. The analyzed studies revealed important impacts at the molecular level, showing that these interventions can be used as effective tools in managing clinical conditions related to chronic stress and inflammation.[1-3,5-8,11]

DISCUSSION

Initially, Sanada et al.[1] documented a significant reduction in levels of pro-inflammatory markers, such as IL-6 and TNF-α, in psychiatric patients receiving mindfulness interventions. These changes are correlated with improvements in conditions like anxiety and depression, indicating that meditative practices can modulate inflammatory pathways associated with emotional disorders. Furthermore, the data highlighted that stress reduction is accompanied by changes in neuroendocrine markers, such as ACTH, suggesting that mindfulness can regulate the hypothalamic-pituitary-adrenal (HPA) axis, whose dysfunction is frequently associated with psychiatric disorders. These findings reinforce the role of mindfulness as an effective and complementary non-pharmacological approach in therapeutic contexts.

In addition, the epigenetic changes observed by Álvarez-López et al.[3] and Chaix et al.[11] offered a deeper understanding of the molecular mechanisms involved. These studies revealed that intensive mindfulness practices induce changes in the methylation of critical genes related to inflammation, such as TNF and RIPK2, and promote chromatin remodeling, including histone modification. Such changes are fundamental for regulating inflammatory, immunological, and cellular aging pathways, indicating that meditative practices have a direct impact on the human epigenome. The study by Chaix et al.[11], in particular, showed that even one day of intensive practice resulted in 61 differential DNA methylation changes, highlighting the rapidity and effectiveness of these interventions.

Regarding cardiovascular health and cellular longevity, Lin et al.[5] demonstrated that practices based on the relaxation response, such as meditation and guided relaxation, increase telomerase activity and regulate miRNAs associated with stress and inflammation. These molecular markers are known to play essential roles in protecting DNA against aging and strengthening vascular health, especially in patients with a history of heart disease. Similarly, Saban et al.[4] discussed how early adversities and cumulative social stress are associated with pro-inflammatory epigenetic signatures that increase the risk of cardiovascular diseases. In this context, mindfulness interventions can reverse these signatures, reducing health inequalities and preventing chronic conditions associated with stress.

The results also highlight the impact of mindfulness on cognitive performance and mental health. Studies such as that by Risatti et al.[9] revealed that BDNF gene methylation, crucial for synaptic plasticity and memory, is beneficially modulated by mindfulness practice. These changes are directly related to the reduction of perceived stress levels, promoting a more favorable epigenetic environment for learning and short-term memory. This relationship is especially relevant in populations under high stress loads, such as teachers and students, where anxiety is often a limiting factor for academic performance.

Additionally, Kripalani et al.[2] demonstrated that mind-body therapies, including yoga and mindfulness meditation, reduce the methylation of inflammatory genes, such as TNF, in women experiencing chronic stress, promoting greater epigenetic stability and emotional health. These practices were also associated with a significant improvement in emotional response and the ability to face challenging situations, strengthening their potential as tools for enhancing emotional resilience in educational and professional environments.

Finally, the findings of Kaliman et al.[7] and Kaliman et al.[10] on the influence of multimodal interventions in vulnerable populations, such as adolescents with adverse childhood experiences, emphasize the ability of mindfulness to promote beneficial epigenetic changes. These combined programs, which include mindfulness and artistic therapy, resulted in changes in the methylation of genes related to stress, inflammation, and endocrine processes, significantly improving symptoms of post-traumatic stress disorder (PTSD) and levels of mindfulness.

CONCLUSION

It is concluded, therefore, that mindfulness practices present a transformative and multifaceted impact, integrating the advances of epigenetic science with ancient meditative knowledge, promoting not only balance between body and mind but also positively interfering with the molecular mechanisms that regulate inflammation and stress. This systematic review demonstrated that mindfulness-based interventions are associated with epigenetic modulation of inflammatory genes, such as TNF, IL-6, and RIPK2, through altering DNA methylation patterns, resulting in relevant anti-inflammatory and neuroprotective effects.

These findings point to the potential of mindfulness as an effective complementary intervention in preventive medicine, especially in populations with psychiatric disorders, cardiovascular diseases, and chronic inflammatory states. Although this strategy is already included among Therapeutic Resources in the SUS (Brazil's public healthcare system),[14] it is crucial to expand its dissemination and implementation to ensure that more individuals benefit from its effects. By incorporating mind-body strategies more broadly into public health policies, we not only promote individual well-being but also contribute to the sustainability of healthcare systems, given the increase in diseases related to stress and modern lifestyles.

As new epigenetic analysis technologies advance, there is an urgent need for studies with larger samples, methodological standardization, and long-term follow-up to consolidate the clinical applicability of mindfulness. With the strengthening of evidence and the implementation of accessible and culturally adapted programs, mindfulness can play a central role in transforming contemporary therapeutic practices, contributing to a more holistic, humanized, and effective approach to health in the 21st century.

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