



Review Article

A Comprehensive Review of 16 Existing Reviews that Investigate the Influence of Stress on the Onset and Exacerbation of Autoimmune Diseases

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Abstract

This comprehensive review presents a compelling synthesis of multiple articles, establishing a strong association between autoimmune diseases and stress exposure. The study explores the role of stress as a potential factor in the development and progression of autoimmune conditions, shedding light on its impact on immune responses. Autoimmune diseases result from the immune system mistakenly attacking the body's own tissues, and growing evidence suggests that psychological stress may play a role in their development and exacerbation. The review synthesizes evidence from 16 existing articles that investigate the association between stress-related disorders and autoimmune conditions. These studies investigate various forms of stress experienced during childhood and adolescence, the genetic associations between stress-related disorders and autoimmune diseases, and the psychosocial impact of autoimmune conditions. Psychosocial factors are found to significantly influence the onset, course, and severity of autoimmune disease, with stress triggering and exacerbating symptoms in affected individuals. The evidence overwhelmingly suggests that individuals with autoimmune conditions experience higher stress levels compared to those without the disease. The objective is to understand the association between stress-related disorders and subsequent autoimmune disease and to explore the impact of stress on inflammation across the lifespan. Psychosocial factors are found to significantly influence the onset, course, and severity of autoimmune disease, with stress triggering and exacerbating symptoms in affected individuals. This review emphasizes the profound impact of psychosocial factors on the quality of life of individuals with autoimmune diseases, further underscoring the importance of stress management in their care. Stress management emerges as a crucial aspect of effective autoimmune disease prevention and management, offering potential benefits for patients' overall well-being.

Keywords: Autoimmune disease; Collaboration among healthcare professionals; Stress

Background

Autoimmune diseases (ADs) are growing health challenges that increasingly affect populations globally. These complex disorders manifest when the immune system mistakenly attacks the body's own cells, causing a cascade of inflammatory responses that can seriously impair physical health. Research into the etiology of ADs indicates that they arise from an interplay between genetic predispositions and various environmental factors. Among these, psychological stress emerges as a significant contributor, leading to a growing field of research that seeks to understand its role in both the genesis and progression of autoimmune conditions. This comprehensive review draws on a variety of scientific sources and synthesizes key findings from 16 prominent articles published in esteemed journals such as this comprehensive review synthesizes key findings from 16 seminal articles published in esteemed journals such as *Autoimmunity Reviews*, *JAMA*, and *Nature Reviews Rheumatology* [1-3]. The methods used in these original studies range from systematic reviews and meta-analyses to longitudinal cohort studies. These studies offer an in-depth investigation into how different forms of psychological stress—be it due to socioeconomic disadvantages, familial discord, early-life traumas, or the subjective experience of stress—may influence autoimmunity. In particular, the studies look at physiological mechanisms like the hypothalamic-pituitary-adrenal (HPA) axis, which mediates the body's stress response and interacts intricately with the immune system [4-6].

The relevance of investigating the relationship between stress and autoimmune diseases is underscored by emerging evidence that suggests stress-induced mechanisms could serve as potential triggers or exacerbators of autoimmune responses. Given that autoimmune conditions can lead to chronic inflammation and a broad array of health complications, understanding the role of stress becomes imperative. Such insights not only deepen our understanding of the underlying mechanisms but also pave the way for potential therapeutic interventions aimed at managing stress. This background section aims to provide a solid foundation for the for the extensive review that follows. It highlights the critical importance of evaluating the impact of stress-related factors on autoimmune diseases, thereby illuminating potential avenues for more effective, multidisciplinary approaches to managing these complex conditions. It also recognizes the urgent need for further research to delineate the intricate pathways through which stress affects autoimmune diseases, thereby laying the groundwork for future investigations [7-10].

Methods

To provide a robust and nuanced understanding of the relationship between stress and autoimmune diseases, this comprehensive review uses a multifaceted approach in its methodological framework.

Database Search and Selection Criteria

A systematic search was conducted across academic databases, primarily PubMed and Scopus, covering a range of articles published from 1981 to 2022. The selection of keywords aimed for specificity and breadth, using terms such as stress, autoimmune diseases, inflammation, psychosocial impact and stress management. A set of inclusion criteria was developed to filter the studies; each article needed to clearly focus on exploring the link between stress and autoimmune diseases [11-14].

Methodological Assessment

Once the initial set of articles was identified, each was carefully evaluated based on several points: methodological rigor, sample size, statistical significance, and the academic standing of the journal. These criteria ensured that only articles published in reputable journals and with robust research methods were included in this review.

Types of Studies Reviewed

The 16 selected articles demonstrated a range of research designs: systematic reviews, meta-analyses, large population-based cohort studies, and retrospective case-control studies. Different aspects were investigated in these studies, such as the influence of stress during developmental phases (childhood and adolescence), psychosocial factors affecting autoimmune diseases, and the role of stress in modulating inflammatory responses.

Cohort and Case-Control Methodologies

In studies that used a population-based cohort design, the focus was particularly on individuals diagnosed with stress-related disorders. These studies often included a matched control group of unexposed individuals to provide a more nuanced understanding of the relationship under investigation. Case-control studies, on the other hand, often examined the incidence of stressful life events prior to the diagnosis of autoimmune diseases, providing a temporal dimension to the relationship.

Data Gathering Techniques

Validated questionnaires were often used to delve into specific life events that may have acted as stressors, thereby providing a qualitative layer to the primarily quantitative data. This compre-

hensive approach facilitated the identification of both environmental and occupational stress factors and how they may intersect with immune system function and the neuroendocrine system.

Meta-Analytic Procedures

Studies using meta-analytic procedures synthesized data across multiple research papers to offer an aggregate view of the evidence, increasing the weight and reliability of the findings.

In conclusion, this review uses a range of research methods to create a multifaceted exploration of stress's influence on autoimmune diseases. Through rigorous selection and analytical processes, it assembles a substantial body of evidence, offering a synthesized yet detailed view of the subject.

Results

This review offers a structured synthesis of findings from 16 key articles exploring the multifaceted relationship between stress and autoimmune diseases (AD). Our goal is to condense a wealth of data into four critical dimensions: stress-inflammation relationships, genetic associations, psychosocial effects, and stress management.

The relationship between stress and inflammation

The link between early life stress and later life inflammation has been proven in several reviews. Chronic stress, especially during developmental years, was found to alter immune system function, leading to a state of persistent inflammation. In particular, a meta-analysis of the study published in *Autoimmunity Reviews* identified that childhood and adolescent stress significantly correlated with increased inflammatory markers in adulthood, providing a potential link to autoimmune diseases.

Genetic Associations

Geographical differences in the prevalence of autoimmune diseases, as observed in the reviewed articles, suggest the potential for genetic susceptibility. These genetic factors, especially when exposed to environmental stressors, may act as catalysts for the onset of AD. For example, reviews highlighted the role of genetic predispositions in combination with stress-induced disturbances in cytokine homeostasis.

Psychosocial Impact

A number of reviews highlighted the emotional and psychological toll that autoimmune diseases cause. A study aptly named *The Psychosocial Impact of Autoimmune Disease* illustrated that those affected by AD are more susceptible to experiencing anxiety, depression and social isolation. These psychosocial factors negatively affect the quality of life and contribute to the severity of the disease. In addition, the study found that the rate of ADs is increasing annually by approximately 20%, accentuating the urgency of public health interventions.

Stress Management

The role of stress management as a preventive or mitigating measure for autoimmune diseases was developed in several articles. Strategies such as mindfulness-based interventions emerged as potentially effective approaches. Despite this, gaps remain in integrating these stress management techniques into conventional medical treatment protocols for AD.

Additional Results

A study published in *JAMA*, conducted on a large Swedish cohort, found a moderate but still significant association between stress-related disorders and autoimmune diseases, with PTSD patients showing increased susceptibility. This underscores the need for targeted interventions for individuals with a history of trauma. Summary of reviews collectively supports a compelling link between stress and autoimmune diseases, manifested through altered inflammatory responses and possible genetic triggers. The psychosocial consequences on individuals with AD further demonstrate the need for integrated care approaches. Despite the strength of the existing evidence, significant gaps remain, particularly regarding the development and integration of stress management techniques into AD treatment regimens. Future research in this arena could offer key insights for more holistic approaches to managing autoimmune diseases.

The results section highlights that there is a significant association between childhood and adolescent stress and increased inflammation in adulthood, potentially contributing to the development of autoimmune diseases. Additionally, psychosocial factors, such as anxiety, depression, and social isolation, were found to influence the course and severity of autoimmune diseases, impacting individuals' quality of life. Our study highlights the association between major stressful events that occurred before diagnosis of autoimmune disorders. The review emphasizes the interplay between the central nervous system, the hypothalamic-pituitary-adrenal axis, and the immune system in response to stress. Stressors, both environmental and occupational, can affect cytokine homeostasis, potentially contributing to autoimmune-prone status in genetically susceptible individuals. This review reveals a significant increase in autoimmune disease frequencies over time, indicating a potential growing burden of these conditions on public health. The studies highlight the growing evidence that psychological factors may influence the development and course of autoimmune diseases, emphasizing the need for more research and effective psychological interventions. The study highlights the importance of early intervention and support to mitigate the effects of stress and reduce the risk of inflammation-related health conditions later in life [15,16].

Conclusions

Our comprehensive review of 16 prominent articles convincingly illustrates the intricate relationship between psychological stress and autoimmune diseases (AD). It highlights how stress, especially when experienced early in life, sets the stage for persistent inflammatory responses that can culminate in autoimmune diseases in adulthood. In addition, the review highlights the psychosocial burden carried by individuals with AD, affecting their psychological well-being and overall quality of life. The review strongly advocates an integrated approach to stress management as a cornerstone in the treatment of autoimmune diseases. By synthesizing evidence across studies, it becomes clear that stress management is not just an adjunct but rather an essential part of effective patient care. Recommended techniques for stress management include mindfulness-based methods, cognitive behavioral therapies, and other psychosocial interventions. Given the multifaceted nature of the relationship between stress and autoimmune diseases, our review highlights the critical need for a multidisciplinary medical team. This team should involve health professionals from different specialties and also integrate the expertise of psychologists and social workers. Such comprehensive care could address not only the physiological but also the emotional and psychological dimensions that characterize autoimmune diseases, thereby significantly improving patient outcomes.

While the reviewed articles lay a significant foundation, they also reveal gaps that future research should aim to fill. Specifically, future work should delve into elucidating the mechanisms behind the stress-autoimmunity link. As the prevalence of AD shows an upward trajectory, there is an urgent need for research focused on innovative therapeutic strategies, especially those involving stress management and psychosocial interventions. Our review presents a compelling argument for the influential role of stress in the onset and progression of autoimmune diseases. By offering practical recommendations for integrating stress management into patient care, the review makes an indispensable contribution to the existing literature. The advocacy for further research accentuates the necessity to advance our understanding of this intricate relationship in order to optimize patient outcomes, quality of life, and public health at large.

Limitation

Although our comprehensive review provides significant insights into the relationship between stress and autoimmune diseases, it is not without limitations. The primary limitations stem from the inherent quality and reporting standard of the reviews included in our analysis. Some reviews did not provide explicit information on sample sizes, and there was a variable degree of rigor in the studies they included. These factors introduce a level of uncertainty which makes definitive conclusions challenging.

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