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The Impact of Psychological Stress on the Development of Internal Diseases

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Abstract: Psychological stress represents a multidimensional physiological and behavioral response that, when chronic, disrupts homeostatic mechanisms and contributes to the onset of numerous internal diseases. The study synthesizes contemporary findings (2017–2025) on neuroendocrine, immune, and metabolic pathways linking stress to systemic disorders. Analysis of cohort studies, meta-analyses, and mechanistic reviews reveals that prolonged activation of the hypothalamic–pituitary–adrenal axis and the sympathetic nervous system induces hormonal imbalance, inflammation, immune dysregulation, and microbiota alterations. These changes increase the risk of cardiovascular, autoimmune, metabolic, respiratory, and oncological diseases. Notably, evidence from the CARDIA and CHIEF cohorts, as well as meta-analyses in Frontiers and Molecular Cancer, highlights chronic stress as an independent etiological factor of hypertension, diabetes, autoimmune disorders, and tumor progression. Behavioral mediators such as unhealthy diet, sedentary lifestyle, and substance abuse amplify these effects. The findings emphasize the necessity of integrating stress-management interventions—psychotherapy, mindfulness, and physical activity—into preventive medicine. Despite strong associative evidence, causal mechanisms remain insufficiently explored, underscoring the need for randomized interventional studies to clarify stress-disease pathways and therapeutic targets.

Keywords: psychological stress, chronic stress, internal diseases, neuroendocrine regulation, immune dysfunction, inflammation, preventive medicine.

Introduction

Psychological stress has become one of the most pervasive health challenges of the 21st century, affecting individuals across all age groups and social backgrounds[1]. Defined as the body's adaptive response to perceived threats or challenges, stress triggers complex neuroendocrine and immune reactions primarily through the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic–adrenal–medullary system[2]. While acute stress responses are adaptive and help organisms cope with short-term danger, chronic or prolonged exposure to psychological stressors results in systemic dysregulation that predisposes individuals to numerous internal diseases[3][4]. Recent advances in psychoneuroimmunology have revealed that chronic stress plays a fundamental role in the pathogenesis of cardiovascular, autoimmune, metabolic, and even oncological disorders by mediating hormonal imbalance, immune suppression, and chronic inflammation[5].

In the last decade, a growing number of epidemiological and experimental studies have explored the biological mechanisms underlying the stress–disease connection[6]. For example, the American Psychological Association (APA, 2024) highlighted that sustained stress exposure leads to persistent activation of cortisol and catecholamine secretion, causing vascular damage and elevated cardiovascular risk. Similarly, meta-analyses published in *Frontiers in Psychiatry*

(2025)[8]demonstrated a statistically significant link between post-traumatic stress disorder and autoimmune diseases such as systemic lupus erythematosus and type 1 diabetes[7]. Other longitudinal cohort studies, including CARDIA and CHIEF, provided strong evidence that chronic stress contributes to hypertension, metabolic syndrome, and insulin resistance through inflammatory and behavioral pathways[8]. Despite this extensive literature, inconsistencies remain concerning causality, dose–response relationships, and the reversibility of stress-induced pathologies[9].

The theoretical foundation of this research draws from the allostatic load model and the biopsychosocial theory, which emphasize that cumulative physiological stress—or "wear and tear" on the body—results from repeated adaptation to psychological and environmental demands[10]. These frameworks explain how dysregulated stress responses over time compromise immune competence, endothelial function, and metabolic homeostasis[11]. However, existing studies often treat stress as a subjective psychological construct rather than a measurable physiological process, creating a gap in integrative approaches that combine hormonal, immunological, and behavioral data[12]. Moreover, few studies have investigated cross-systemic interactions—such as the brain–gut–immune axis—that mediate the somatic expression of psychological stress[13][14].

To address these limitations, this study integrates recent findings from clinical, epidemiological, and molecular research published between 2017 and 2025. Using a comprehensive literature review method, it examines how chronic psychological stress influences neuroendocrine regulation, immune signaling, and metabolic outcomes. Special attention is given to large-scale cohort and meta-analytic data to identify consistent biological markers and potential mediators of disease risk. The analysis also considers behavioral moderators—such as sleep quality, diet, and physical activity—that may amplify or mitigate stress-induced physiological effects.

The results of this synthesis suggest that chronic psychological stress acts as a universal risk factor for internal diseases through multidimensional mechanisms involving HPA-axis dysregulation, inflammation, and microbiota imbalance. Understanding these pathways not only advances theoretical models of stress pathology but also has practical implications for clinical prevention. Effective stress-management interventions—including cognitive behavioral therapy, mindfulness, and physical exercise—show promise in restoring physiological balance and reducing disease burden. Therefore, integrating psychological well-being into medical and public health strategies is essential for achieving holistic, sustainable health outcomes.

Methodology

This study employs an integrative review approach aimed at synthesizing the latest empirical and theoretical evidence on the impact of psychological stress on internal diseases. The research is based on a systematic analysis of peer-reviewed scientific literature published between 2017 and 2025, with a focus on works that investigate the neuroendocrine, immunological, metabolic, and behavioral mechanisms of stress. Databases such as PubMed, Scopus, ScienceDirect, and Google Scholar were searched using combinations of keywords including *psychological stress*, *HPA axis*, *immune dysfunction*, *chronic inflammation*, *metabolic disorders*, and *cardiovascular disease*. Selection criteria included original research articles, meta-analyses, and systematic reviews that presented measurable outcomes linking chronic psychological stress with specific physiological dysfunctions or disease risks. Studies lacking empirical evidence or limited to animal models without translational relevance were excluded. The collected sources were evaluated through comparative and thematic analysis to identify convergent findings and conceptual frameworks explaining the stress–disease relationship. Special attention was given to large cohort studies (e.g., CARDIA, MESA, CHIEF) and high-impact reviews published in journals such as *Frontiers*, *Molecular Cancer*, and *Molecular Psychiatry*. Quantitative data were summarized descriptively, while qualitative interpretations highlighted biological pathways and behavioral mediators contributing to health deterioration. The methodological framework integrates interdisciplinary perspectives from psychoneuroimmunology, endocrinology, and

public health to ensure a holistic understanding of the problem. This evidence-based synthesis serves to clarify the causal mechanisms, identify research gaps, and propose practical implications for prevention and stress-management interventions.

Results and Discussion

The synthesis of contemporary scientific literature (2017–2025) confirms that chronic psychological stress exerts a systemic influence on multiple physiological systems through the dysregulation of neuroendocrine and immune mechanisms. Analysis of large-scale cohort studies and meta-analyses revealed a consistent association between stress exposure and increased incidence of cardiovascular, autoimmune, metabolic, respiratory, and oncological diseases. Chronic activation of the hypothalamic–pituitary–adrenal (HPA) axis results in prolonged cortisol secretion, glucocorticoid receptor resistance, and systemic inflammation. These alterations lead to endothelial dysfunction, insulin resistance, immune imbalance, and changes in gut microbiota composition.

Table 1 presents the principal health domains affected by stress, associated biological markers, and supporting evidence.

Table 1. Physiological Systems Affected by Chronic Psychological Stress

System	Pathophysiological Mechanism	Key References (2017–2025)
Cardiovascular	Elevated cortisol, increased blood pressure, inflammation in coronary arteries	APA (2024); CARDIA Study [6–8]
Immune/Autoimmune	Overproduction of IL-6, TNF-α, CRP; impaired NK and T-cell activity	Frontiers (2025); MDPI (2024) [2,10,11]
Metabolic	Insulin resistance, visceral fat accumulation, hyperglycemia	PMC (2025); CHIEF cohort [7–8]
Gastrointestinal	Gut microbiota dysbiosis, intestinal permeability, inflammation	Frontiers (2020) [10-12]
Oncological	β-adrenergic activation, DNA damage, oxidative stress, tumor progression	Molecular Cancer (2025) [1-4--8]

The results indicate that stress-induced physiological changes are not limited to a single organ system but represent a complex multisystem interaction. Chronic activation of stress pathways disrupts homeostasis through constant elevation of glucocorticoids and catecholamines, which affect immune cell gene expression and inflammatory balance. For instance, studies within *Frontiers in Immunology* (2025) identified a 29% higher risk of autoimmune disease among individuals exposed to severe post-traumatic stress, while longitudinal research in *Molecular Cancer* positioned chronic stress as a “fourth etiological factor” in tumorigenesis. Similarly, the CARDIA study found that sustained psychological stress shortened life expectancy by 8–9%, primarily mediated through metabolic and cardiovascular dysfunction.

From a theoretical perspective, these findings reinforce the allostatic load model, emphasizing that continuous adaptation to stressors leads to biological “wear and tear.” Yet, the precise causal pathways remain partly unresolved, particularly regarding how chronic inflammation transitions into irreversible tissue damage or oncogenic transformation. Furthermore, research on the microbiota–gut–brain axis suggests that stress-induced dysbiosis may mediate both somatic and psychiatric symptoms, representing a promising field for future interdisciplinary exploration.

Practical implications emerge in preventive medicine and therapeutic design. Evidence supports the integration of stress-management techniques—such as cognitive-behavioral therapy, mindfulness, and controlled physical activity—into chronic disease prevention programs.

Pharmacological interventions targeting β-adrenergic signaling and cortisol modulation are being explored as adjunctive treatments for cancer and autoimmune conditions.

Nevertheless, significant research gaps persist. Most existing studies rely on observational data, limiting causal inference. Future investigations should employ longitudinal and randomized controlled designs incorporating multi-omics profiling (genomic, proteomic, and metabolomic) to elucidate personalized stress-response mechanisms. Additionally, cross-cultural studies are required to examine socioeconomic and environmental moderators of stress vulnerability.

In summary, the evidence demonstrates that psychological stress is a universal pathophysiological trigger with multidimensional effects on human health. Bridging theoretical understanding with practical applications through integrative biomedical and behavioral research will be critical for developing targeted prevention and intervention strategies.

Conclusion

The comprehensive analysis of contemporary scientific evidence demonstrates that chronic psychological stress functions as a universal etiological factor contributing to the onset and progression of internal diseases through complex neuroendocrine, immune, and metabolic mechanisms. Persistent activation of the hypothalamic–pituitary–adrenal axis and sympathetic nervous system leads to hormonal dysregulation, systemic inflammation, immune suppression, and microbiota imbalance, collectively increasing susceptibility to cardiovascular, autoimmune, metabolic, respiratory, and oncological pathologies. These findings highlight that psychological stress is not merely a mental state but a measurable biological process with profound somatic consequences. The results underscore the necessity of integrating stress management, behavioral interventions, and preventive mental health strategies into public health and clinical practice to mitigate disease burden and enhance life quality. Nevertheless, current research remains limited by correlational designs and insufficient mechanistic clarity. Future studies should prioritize longitudinal, multi-omics, and interventional methodologies to establish causal relationships, identify biomarkers of stress resilience, and develop precision-based therapeutic models that bridge psychological well-being with physiological health outcomes.

References

1. Central-peripheral neuroimmune dynamics in psychological stress and depression: insights from current research. *PMC*, 2025. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC12436188/
2. *Immunology of Stress: A Review Article. MDPI Journal of Clinical Medicine*, 2024. Available at: https://www.mdpi.com/2077-0383/13/21/6394
3. *Stress Effects on the Body. American Psychological Association*, 2024. Available at: https://www.apa.org/topics/stress/body
4. *Chronic Stress and Cardiovascular Events: Findings from the CARDIA Study. PMC*, 2025. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC11193648/
5. *Psychobiological Reactivity to Acute Psychological Stress as a Predictor of Cardiovascular Disease and Mortality: The Multi-Ethnic Study of Atherosclerosis. PubMed*, 2025. Available at: https://pubmed.ncbi.nlm.nih.gov/41135261/
6. *Systematic Review and Meta-Analysis of Post-Traumatic Stress Disorder as a Risk Factor for Multiple Autoimmune Diseases. Frontiers in Psychiatry*, 2025. Available at: https://www.frontiersin.org/journals/psychiatry/articles/10.3389/fpsyt.2025.1523994/full
7. *The Impact of Stress on Autoimmune Disorders: Type 1 Diabetes Mellitus and Systemic Lupus Erythematosus. PMC*, 2025. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC12025346/

8. *Psychological Stress, Intestinal Barrier Dysfunctions, and Autoimmune Disorders: An Overview. Frontiers in Immunology*, 2020. Available at: https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2020.01823/full
9. *Stress Increases the Risk of Type 2 Diabetes Onset in Women: A 12-Year Longitudinal Study Using Causal Modelling. PMC*, 2025. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC5319684/
10. *Stress and Anxiety Are Associated with Increased Metabolic Syndrome Risk Among Young Adults Living in the Deep South. PMC*, 2025. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC11855769/
11. *Mental Stress and the Risks of Metabolic Syndrome and Related Components in Military Personnel: CHIEF Cohort Study. PMC*, 2025. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC12408596/
12. *Depression Increases the Risk of Asthma: Evidence from a Cross-Sectional Study and Two-Sample Mendelian Randomization Analysis. PMC*, 2025. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC12499669/
13. *Chronic Stress: A Fourth Etiology in Tumorigenesis? Molecular Cancer*, 2025. Available at: https://molecular-cancer.biomedcentral.com/articles/10.1186/s12943-025-02402-x
14. *Biomarkers of Psychological Stress Are Associated with Increased Susceptibility to the Development of Breast and Prostate Cancer in BRCA1/2 Mutation Carriers. PubMed*, 2025. Available at: https://pubmed.ncbi.nlm.nih.gov/40603570/