The Role of Stress, Inflammation, and Depression in Postural Orthostatic Tachycardia: A Psychoneuroimmunology Perspective

Tawana McCou MS
Walden University
School of Health Sciences
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Abstract

Postural Orthostatic Tachycardia Syndrome (POTS) is a chronic autonomic nervous system disorder characterized by tachycardia, dizziness, fatigue, cognitive impairment, and orthostatic intolerance. Increasing evidence suggests that immune dysfunction, chronic inflammation, stress responses, and psychological factors contribute significantly to symptom severity and disease progression. This manuscript examines the relationship between stress, inflammation, depression, and autonomic dysfunction in individuals with POTS through the lens of psychoneuroimmunology (PNI). Additionally, cognitive and behavioral interventions including Cognitive Behavioral Therapy (CBT), Mindfulness-Based Stress Reduction (MBSR), and biofeedback training are explored as potential strategies for improving symptom management and quality of life. The manuscript further emphasizes the importance of interdisciplinary and biopsychosocial approaches to chronic illness management. Findings suggest that psychological stress and immune dysregulation may intensify autonomic symptoms while behavioral interventions may improve coping, emotional regulation, and patient outcomes. Understanding the interaction between psychological and physiological processes within POTS may contribute to more comprehensive treatment approaches and support positive social change within chronic illness care.

Keywords: Psychoneuroimmunology, POTS, autonomic dysfunction, chronic illness, inflammation, stress, depression, cognitive behavioral therapy

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Introduction

Postural Orthostatic Tachycardia Syndrome (POTS) is a chronic autonomic nervous system disorder characterized by an abnormal increase in heart rate when transitioning from a supine to upright position. Symptoms commonly include dizziness, fatigue, tachycardia, orthostatic intolerance, cognitive dysfunction, and chronic pain. Although the exact etiology of POTS remains unclear in many cases, growing evidence suggests that immune dysfunction, chronic inflammation, stress responses, and psychological factors contribute significantly to disease severity and symptom progression.

The chronic and unpredictable nature of POTS often results in substantial physical limitations and psychological distress. Many individuals experience difficulties maintaining daily activities, employment, education, and social functioning due to persistent symptoms. As a result, the condition frequently affects both physical and mental well-being, contributing to increased rates of anxiety, depression, and stress-related symptom exacerbation.

Psychoneuroimmunology (PNI), which examines the interaction between psychological processes, the nervous system, and immune function, provides a useful framework for understanding the complex relationship between stress, inflammation, autonomic dysfunction, and mental health in POTS. Research increasingly demonstrates that chronic stress and immune dysregulation may intensify autonomic symptoms while simultaneously contributing to emotional distress and reduced quality of life.

This manuscript examines the role of stress, inflammation, and depression in POTS while exploring cognitive and behavioral interventions aimed at improving patient outcomes. Particular attention is given to Cognitive Behavioral Therapy (CBT), Mindfulness-Based Stress Reduction (MBSR), and biofeedback training as non-pharmacological approaches to symptom management and chronic illness support.

Methodology

This manuscript utilized a narrative literature review methodology to examine current scholarly research related to Postural Orthostatic Tachycardia Syndrome (POTS), psychoneuroimmunology, stress, inflammation, depression, and behavioral interventions. Literature searches were conducted using scholarly databases including PubMed, PsycINFO, Google Scholar, and CINAHL.

Keywords included “Postural Orthostatic Tachycardia Syndrome,” “POTS,” “psychoneuroimmunology,” “stress response,” “autonomic dysfunction,” “depression,” “inflammation,” “biofeedback,” “mindfulness,” and “cognitive behavioral therapy.” Peer-reviewed journal articles, literature reviews, and clinical studies published primarily between 2021 and

2025 were prioritized to ensure the inclusion of current evidence and emerging perspectives regarding POTS and chronic illness management.

The literature was analyzed thematically, with key areas categorized into autonomic dysfunction, immune dysregulation, stress responses, depression, cognitive and behavioral interventions, and interdisciplinary chronic illness management.

Theoretical Framework

This manuscript is conceptually grounded in the biopsychosocial model and psychoneuroimmunology (PNI). The biopsychosocial model emphasizes the interaction between biological, psychological, and social factors in influencing health outcomes, while PNI examines the relationship between psychological processes, nervous system functioning, and immune responses.

Within POTS, these frameworks are particularly relevant because physiological symptoms are often influenced by psychological stress, inflammatory responses, and emotional regulation. Chronic stress activates the hypothalamic-pituitary-adrenal (HPA) axis, resulting in increased cortisol production and immune dysregulation. These physiological changes may exacerbate autonomic dysfunction, increase inflammation, and intensify symptom severity among individuals with POTS.

The integration of PNI into chronic illness management supports the development of interdisciplinary treatment approaches that address both physiological and psychological dimensions of care. Cognitive and behavioral interventions may improve patient outcomes by reducing stress responses, strengthening coping mechanisms, and improving emotional well-being.

Postural Orthostatic Tachycardia Syndrome (POTS)

Postural Orthostatic Tachycardia Syndrome (POTS) is an autonomic condition characterized by an excessive increase in heart rate when moving from a supine to standing position without a significant decrease in blood pressure. Symptoms commonly include dizziness, fainting, fatigue, orthostatic intolerance, chronic pain, tachycardia, and cognitive impairment commonly referred to as “brain fog.”

The autonomic nervous system regulates involuntary physiological functions including heart rate, blood pressure, digestion, and respiration. Dysregulation of autonomic functioning contributes significantly to symptom presentation among individuals with POTS (Stuart et al., 2025). Although the underlying causes of POTS vary, the condition has been associated with viral infections, autoimmune processes, chronic fatigue syndrome, physical trauma, and post-viral syndromes including post-acute COVID-19 conditions.

The complexity of POTS often makes diagnosis and treatment challenging. Many patients experience delayed diagnosis due to symptom overlap with anxiety disorders, chronic fatigue conditions, and other autonomic disorders. Consequently, comprehensive and interdisciplinary approaches to treatment are essential for effective symptom management.

Immune Dysfunction and Inflammation in POTS

Emerging evidence suggests that immune dysfunction and chronic inflammation play important roles in the development and progression of POTS. One proposed mechanism involves the production of autoantibodies targeting adrenergic receptors involved in blood pressure and heart rate regulation. These autoantibodies may impair autonomic functioning and contribute to symptoms such as tachycardia and orthostatic intolerance (Ghazal et al., 2025).

Chronic inflammation has also been observed among individuals with POTS. Elevated levels of inflammatory cytokines including TNF-alpha and interleukin-6 (IL-6) may contribute to endothelial dysfunction, cardiovascular instability, and symptom exacerbation (Mahdi et al., 2023). These inflammatory responses may further complicate autonomic regulation and intensify fatigue, dizziness, and cognitive dysfunction.

The relationship between immune dysfunction and autonomic instability highlights the importance of comprehensive treatment approaches addressing both physiological and psychological factors associated with chronic illness management.

Stress Responses and Autonomic Dysfunction

Psychological stress significantly influences autonomic functioning and may exacerbate symptoms among individuals with POTS. Activation of the hypothalamic-pituitary-adrenal (HPA)

axis during stress responses increases cortisol production and contributes to inflammatory processes and immune dysregulation (Ishizaki et al., 2022).

Stress-related hormonal changes may intensify tachycardia, dizziness, fatigue, and orthostatic intolerance among individuals with POTS. Furthermore, chronic stress may contribute to a bidirectional cycle in which symptom severity increases emotional distress while psychological distress further exacerbates physiological symptoms.

Mahdi et al. (2023) reported that chronic stress may contribute to the production of pro-inflammatory cytokines, further intensifying autonomic dysfunction and symptom severity. These findings support the importance of stress management interventions within comprehensive POTS treatment plans.

Behavioral interventions aimed at reducing stress responses may improve emotional regulation, reduce inflammatory responses, and strengthen patient coping mechanisms. Cognitive Behavioral Therapy (CBT), mindfulness practices, and biofeedback interventions have demonstrated potential benefits in reducing stress-related symptom exacerbation among individuals with chronic illnesses.

Depression and Psychological Distress in POTS

Depression represents one of the most common psychological comorbidities associated with POTS. The chronic and debilitating nature of the condition frequently contributes to emotional distress, reduced quality of life, social isolation, and impaired functioning.

Tsai Owens et al. (2024) found that individuals with POTS experience significantly higher rates of depression and cognitive difficulties compared to the general population. Depression may intensify autonomic symptoms by increasing inflammation, disrupting emotional regulation, and worsening physiological stress responses.

Additionally, cognitive dysfunction or “brain fog” commonly reported among individuals with POTS may contribute to frustration, emotional exhaustion, and reduced psychological resilience. The overlap between autonomic dysfunction, chronic stress, inflammation, and depression suggests a shared pathophysiological relationship requiring interdisciplinary treatment approaches.

Recognizing and addressing mental health concerns among individuals with POTS is critical for improving both psychological and physical health outcomes.

Cognitive and Behavioral Interventions

Cognitive Behavioral Therapy (CBT)

Cognitive Behavioral Therapy (CBT) is a structured psychotherapeutic intervention designed to address maladaptive thought patterns, emotional distress, and behavioral responses associated with chronic illness. CBT may improve coping skills, emotional regulation, symptom management, and treatment adherence among individuals with POTS.

Research suggests that CBT may reduce depressive symptoms, anxiety, and stress-related symptom exacerbation among individuals with chronic illnesses (Tsai Owens et al., 2024). Group CBT interventions may also provide social support and reduce feelings of isolation commonly experienced among individuals living with chronic conditions.

Mindfulness-Based Stress Reduction (MBSR)

Mindfulness-Based Stress Reduction (MBSR) combines mindfulness meditation, body awareness, and stress reduction techniques aimed at improving emotional well-being and reducing physiological stress responses. MBSR may help individuals with POTS manage anxiety, emotional distress, and autonomic symptom exacerbation.

Group mindfulness programs may additionally provide social support and foster a sense of community among individuals living with chronic illness. These interventions support the integration of psychological and physiological symptom management strategies.

Biofeedback Training

Biofeedback training teaches individuals to regulate physiological responses such as heart rate variability, muscle tension, and blood pressure using real-time physiological feedback. Biofeedback may improve autonomic regulation and reduce orthostatic intolerance symptoms among individuals with POTS.

Heart rate variability (HRV) biofeedback has demonstrated potential benefits in improving autonomic functioning and reducing symptom severity. Neurofeedback interventions may additionally improve cognitive functioning and emotional regulation while reducing stress and anxiety symptoms.

Biofeedback represents a promising non-pharmacological intervention supporting active patient participation in chronic illness management.

Positive Social Change

Understanding the relationship between stress, inflammation, immune dysfunction, and psychological distress within POTS may contribute to improved chronic illness management and healthcare accessibility. Many individuals with POTS experience delayed diagnosis, misunderstanding, and limited access to comprehensive interdisciplinary care.

By promoting awareness of psychoneuroimmunology and the interconnected nature of chronic illness, healthcare systems may improve treatment approaches that address both physiological and psychological dimensions of care. Integrating behavioral health interventions into chronic illness management may strengthen patient outcomes, reduce stigma, and improve quality of life.

This manuscript supports positive social change by emphasizing holistic and patient-centered approaches to chronic illness management while advocating for increased awareness regarding the psychological impact of autonomic disorders.

Limitations

Several limitations should be considered when interpreting the findings presented in this manuscript. First, POTS remains a relatively under-researched condition, and evolving scientific understanding may influence future interpretations regarding autonomic dysfunction and immune involvement.

Second, variability in symptom presentation and treatment responses among individuals with POTS may limit the generalizability of certain findings. Additionally, much of the current literature regarding behavioral interventions within POTS management remains preliminary, highlighting the need for additional longitudinal research.

Finally, this manuscript utilized a narrative review approach rather than a systematic review methodology, which may introduce selection bias despite efforts to incorporate current and diverse scholarly literature.

Future Research Recommendations

Future research should further examine the relationship between autonomic dysfunction, chronic inflammation, psychological stress, and immune dysregulation within POTS. Longitudinal studies evaluating behavioral interventions such as CBT, MBSR, and biofeedback training may strengthen understanding regarding long-term treatment outcomes.

Additional research should also explore the effectiveness of interdisciplinary and accessibility-centered healthcare approaches addressing both physiological and psychological dimensions of chronic illness management.

As understanding of psychoneuroimmunology continues to expand, future investigations may contribute to more comprehensive and patient-centered approaches for individuals living with autonomic disorders.

Conclusion

Postural Orthostatic Tachycardia Syndrome (POTS) is a complex chronic illness influenced by autonomic dysfunction, immune dysregulation, chronic inflammation, stress responses, and psychological distress. The findings presented throughout this manuscript demonstrate the importance of understanding the interconnected relationship between physiological and psychological processes within chronic illness management.

Behavioral interventions including Cognitive Behavioral Therapy, Mindfulness-Based Stress Reduction, and biofeedback training offer promising non-pharmacological approaches for improving symptom management, emotional regulation, and quality of life among individuals with POTS.

By integrating psychoneuroimmunology, behavioral science, and interdisciplinary healthcare approaches, providers may develop more comprehensive treatment strategies that address the multifaceted nature of chronic illness. Ultimately, increasing awareness regarding the psychological and physiological dimensions of POTS may contribute to improved patient outcomes, stronger healthcare support systems, and meaningful positive social change.

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