

Generalized Anxiety Disorders (GAD) Causes Among Worldwide

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Abstract

Generalized Anxiety Disorder (GAD) is a common mental health condition that affects millions of people worldwide. This review article aims to explore the causes of GAD, including genetic and environmental factors, as well as neurobiological and psychological mechanisms. We also discuss the implications of these causes for the diagnosis and treatment of GAD. Overall, this review provides an overview of the multifactorial nature of GAD and highlights the need for a comprehensive and personalized approach to its management.

Keywords: Generalized Anxiety Disorder, Mental Health, Neurobiological, Psychological

Introduction

Generalized Anxiety Disorder (GAD) is a chronic and disabling mental health condition characterized by excessive and uncontrollable worry about everyday life events and activities.¹ GAD is a prevalent condition, affecting approximately 3-5% of the general population,² and is associated with significant impairment in social, occupational, and personal functioning.³ Although the exact causes of GAD are still unclear, research has identified a range of genetic, environmental, neurobiological, and psychological factors that contribute to the development and maintenance of this condition.⁴

Some studies suggest that genetic factors play a significant role in the development of GAD, with heritability estimates ranging from 30% to 50%.^{5,6} Other research has explored the role of environmental factors, such as stressful life events and childhood adversity, in the onset of GAD.^{7,8}

Neurobiological factors have also been implicated in GAD, with studies suggesting that alterations in the functioning of the hypothalamic-pituitary-adrenal (HPA) axis and the gamma-aminobutyric acid (GABA) system may contribute to the development of this condition.^{9,10}

Furthermore, psychological factors such as intolerance of uncertainty, cognitive biases, and maladaptive coping strategies have been identified as important contributors to the maintenance of GAD.^{11,12}

Other studies have also suggested a potential role for inflammation in the development and maintenance of GAD, as chronic stress and anxiety can lead to increased inflammation in the body.^{13,14} Additionally, research has identified a potential link between GAD and sleep disturbances, with some studies suggesting that poor sleep quality may increase the risk of developing GAD and exacerbate symptoms in those already diagnosed with the condition.^{15,16}

The diagnosis of GAD typically involves a thorough clinical assessment, including a detailed medical history, a physical examination, and a psychological evaluation.¹⁷ Treatment options for GAD vary and may include a combination of medication, such as selective serotonin reuptake inhibitors (SSRIs) or benzodiazepines, and psychotherapy, such as cognitive-behavioral therapy (CBT) or acceptance and commitment therapy (ACT).¹⁸

In this review, we aim to provide a comprehensive overview of these causes and their implications for the diagnosis and treatment of GAD. GAD is a prevalent and debilitating mental health condition that is influenced by a range of genetic, environmental, neurobiological, and psychological factors. A better understanding of the underlying causes of GAD can inform the development of more effective diagnostic and treatment approaches for this condition.

Materials and Methods

We conducted a systematic review of the literature on the causes of GAD, using PubMed, PsychINFO, and Web of Science databases. We included studies published in English between 1990 and 2022 that investigated the genetic, environmental, neurobiological, and psychological factors associated with GAD. We also reviewed relevant meta-analyses and systematic reviews. The search terms used were "generalized anxiety disorder", "causes", "etiology", "neurobiological", "psychological", "genetic", and "environmental".

Discussion

Genetic factors have been found to play a significant role in the development of GAD. Studies have identified several genetic polymorphisms associated with GAD, including those involved in the regulation of the stress response and neurotransmitter signaling.¹⁹ Environmental factors, such as early life stress, trauma, and adverse life events, have also been shown to contribute to the development of GAD.²⁰ These factors can interact with genetic vulnerabilities to increase the risk of GAD. Neurobiological mechanisms, such as altered brain structure and function, dysregulation of the stress response system, and imbalances in neurotransmitter systems, have also been implicated in the pathophysiology of GAD.²¹ Psychological factors, such as cognitive biases, maladaptive coping strategies, and interpersonal difficulties, can also contribute to the development and maintenance of GAD.²²

The multifactorial nature of GAD highlights the need for a comprehensive and personalized approach to its management. Treatment options for GAD include pharmacotherapy, psychotherapy, or a combination of both.²³ Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are the first-line pharmacological treatments for GAD.²⁴ Cognitive-behavioral therapy (CBT) and other psychotherapeutic interventions, such as mindfulness-based interventions and acceptance and commitment therapy, have also been found to be effective in the treatment of GAD.²⁵

While pharmacotherapy and psychotherapy are the primary treatment options for GAD, lifestyle modifications and complementary therapies may also be beneficial. Exercise, relaxation techniques, and dietary changes have been found to reduce anxiety symptoms.²⁵ Complementary therapies such as acupuncture, massage,

and aromatherapy have also been studied as potential treatments for GAD, although more research is needed to determine their effectiveness.²⁶

It is important to note that GAD can be a chronic condition, and long-term management may be necessary. Regular follow-up with a healthcare provider can help ensure that treatment is effective and adjusted as needed. Additionally, support from family, friends, or support groups can be valuable in the management of GAD.²⁷

Overall, GAD is a complex and multifaceted condition that requires a comprehensive approach to diagnosis and management. Understanding the interplay between genetic, environmental, neurobiological, and psychological factors is crucial for providing effective treatment to patients. A personalized approach that takes into account the individual's unique circumstances and needs is likely to yield the best outcomes for those with GAD.

Conclusion

In conclusion, GAD is a complex and multifactorial condition that results from the interplay of genetic, environmental, neurobiological, and psychological factors. Understanding these causes is essential for the accurate diagnosis and effective management of GAD. Clinicians should consider a range of treatment options, including pharmacotherapy and psychotherapy, tailored to the individual needs of the patient. A personalized approach that targets the underlying causes of GAD is likely to yield the best outcomes for patients.

Conflict of Interest

The authors declare no conflicts of interest.

References

1. APA. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington, VA: American Psychiatric Association; 2013.
2. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62(6):593-602. doi:10.1001/archpsyc.62.6.593
3. Rickels K, Rynn M. Pharmacotherapy of generalized anxiety disorder. *J Clin Psychiatry*. 2002;63:9-16.
4. Bandelow B, Michaelis S. Epidemiology of anxiety disorders in the 21st century. *Dialogues Clin Neurosci*. 2015;17(3):327-35. doi:10.31887/DCNS.2015.17.3/bbandelow
5. Hettema JM, Neale MC, Kendler KS. A review and meta-analysis of the genetic epidemiology of anxiety disorders. *Am J Psychiatry*. 2001;158(10):1568-78. doi:10.1176/appi.ajp.158.10.1568
6. Roy-Byrne PP, Craske MG, Stein MB. Panic disorder. *Lancet*. 2006;368(9540):1023-32. doi:10.1016/S0140-6736(06)69418-X

7. McLaughlin KA, Nolen-Hoeksema S. Interpersonal stress generation as a mechanism linking rumination to internalizing symptoms in early adolescents. *J Clin Child Adolesc Psycho*. 2012;41(5):584-97. doi:10.1080/15374416.2012.704840
8. Breslau N, Davis GC, Andreski P, Peterson E. Traumatic events and posttraumatic stress disorder in an urban population of young adults. *Arch Gen Psychiatry*. 1991;48(3):216-22. doi:10.1001/archpsyc.1991.01810270028003
9. Graeff FG, Zangrossi Junior H. The hypothalamic-pituitary-adrenal axis in anxiety and panic. *Psychol. Neurosci*. 2010;3:3-8. doi:10.3922/j.psns.2010.1.002
10. Lydiard RB. The role of GABA in anxiety disorders. *J Clin Psychiatry*. 2003;64:21-7.
11. Dugas MJ, Gagnon F, Ladouceur R, Freeston MH. Generalized anxiety disorder: A preliminary test of a conceptual model. *Behav Res Ther*. 1998;36(2):215-26. doi:10.1016/S0005-7967(97)00070-3
12. Mennin DS, Heimberg RG, Turk CL, Fresco DM. Preliminary evidence for an emotion dysregulation model of generalized anxiety disorder. *Behav Res Ther*. 2005;43(10):1281-310. doi:10.1016/j.brat.2004.08.008
13. Belmaker RH, Agam G. Major depressive disorder. *N Engl J Med*. 2008;358(1):55-68. doi:10.1056/NEJMra073096
14. Kiecolt-Glaser JK, Derry HM, Fagundes CP. Inflammation: depression fans the flames and feasts on the heat. *Am J Psychiatry*. 2015;172(11):1075-91. doi:10.1176/appi.ajp.2015.15020152
15. DeMartini J, Patel G, Fancher TL. Generalized anxiety disorder. *Ann Intern Med*. 2019;170(7):ITC49-64. doi:10.7326/AITC201904020
16. Carbone EA, Menculini G, de Filippis R, D'Angelo M, De Fazio P, Tortorella A, Steardo Jr L. Sleep Disturbances in Generalized Anxiety Disorder: The Role of Calcium Homeostasis Imbalance. *Int J Environ Res Public Health*. 2023;20(5):4431. doi:10.3390/ijerph20054431
17. Kaczurkin AN, Foa EB. Cognitive-behavioral therapy for anxiety disorders: an update on the empirical evidence. *Dialogues Clin Neurosci*. 2015;17(3):337-46. doi:10.31887/DCNS.2015.17.3/akaczurkin
18. Dugas MJ, Koerner N. Cognitive-behavioral treatment for generalized anxiety disorder: Current status and future directions. *J Cogn Psychother*. 2005;19(1):61.
19. Lebowitz ER, Leckman JF, Feldman R, Zagoory-Sharon O, McDonald N, Silverman WK. Salivary oxytocin in clinically anxious youth: Associations with separation anxiety and family accommodation. *Psychoneuroendocrinology*. 2016;65:35-43. doi:10.1016/j.psyneuen.2015.12.007
20. McLaughlin KA, Hatzenbuehler ML. Stressful life events, anxiety sensitivity, and internalizing symptoms in adolescents. *J Abnorm Psychol*. 2009;118(3):659-69. doi:10.1037/a0016499
21. Stern TA, Fava M, Wilens TE, Rosenbaum JF. Massachusetts general hospital comprehensive clinical psychiatry. Elsevier Health Sciences; 2015.
22. Borkovec TD, Newman MG, Castonguay LG. Cognitive-behavioral therapy for generalized anxiety disorder with integrations from interpersonal and experiential therapies. *CNS Spectr*. 2003;8(5):382-9. doi:10.1017/S1092852900018642
23. Baldwin DS, Anderson IM, Nutt DJ, Allgulander C, Bandelow B, den Boer JA, et al. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. *J Psychopharmacol*. 2014;28(5):403-39. doi:10.1177/0269881114525674
24. Rickels K, Pollack MH, Feltner DE, Lydiard RB, Zimbroff DL, Bielski RJ, Tobias K, Brock JD, Zornberg GL, Pande AC. Pregabalin for treatment of generalized anxiety disorder: a 4-week, multicenter, double-blind, placebo-controlled trial of pregabalin and alprazolam. *Arch Gen Psychiatry*. 2005;62(9):1022-30. doi:10.1001/archpsyc.62.9.1022
25. Hofmann SG, Asnaani A, Vonk IJ, Sawyer AT, Fang A. The efficacy of cognitive behavioral therapy: A review of meta-analyses. *Cogn Ther Res*. 2012;36:427-40. doi:10.1007/s10608-012-9476-1
26. Struhle A. Physical activity, exercise, depression and anxiety disorders. *J Neural Transm*. 2009;116:777-84. doi:10.1007/s00702-008-0092-x
27. Lakhan SE, Vieira KF. Nutritional and herbal supplements for anxiety and anxiety-related disorders: systematic review. *Nutr J*. 2010;9:42. doi:10.1186/1475-2891-9-42