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PANIC DISORDER AS A DETERMINANT OF HYPERTENSION DEVELOPMENT: AUTONOMIC, NEUROBIOLOGICAL, AND BIOPSYCHOSOCIAL MECHANISMS LINKING ACUTE PANIC TO CHRONIC CARDIOVASCULAR DISEASE – REVIEW

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ABSTRACT

Hypertension remains one of the leading global causes of cardiovascular morbidity and mortality. While traditional biomedical risk factors account for substantial risk, increasing evidence suggests that psychological and neurobiological mechanisms contribute significantly to long-term blood pressure regulation. Panic disorder, characterised by recurrent episodes of intense autonomic activation, may represent an under-recognised determinant of sustained hypertension development. This review synthesises epidemiological, autonomic, neurophysiological, inflammatory, and biopsychosocial evidence linking panic disorder with hypertension. Converging evidence indicates altered sympathetic firing patterns, enhanced baroreflex gain, increased blood pressure variability, recurrent hypertensive surges, endothelial dysfunction, and cumulative allostatic load. Longitudinal data demonstrate elevated risk of incident hypertension among individuals with panic disorder independent of conventional cardiovascular risk factors. Integrating mental health assessment into cardiovascular prevention strategies may provide an innovative interdisciplinary approach to reducing global disease burden.

KEYWORDS

Panic Disorder, Hypertension, Sympathetic Nervous System, Blood Pressure Variability, Allostatic Load, Biopsychosocial Model

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Introduction

Hypertension remains one of the most significant contributors to global cardiovascular morbidity and mortality. Despite decades of biomedical research, essential hypertension continues to defy complete mechanistic explanation. Classical risk factors such as age, genetic predisposition, obesity, dietary sodium intake, and sedentary behaviour account for substantial epidemiological variance; however, they do not fully explain individual susceptibility, variability in disease onset, or resistance to treatment. Increasingly, attention has turned toward central nervous system regulation, psychosocial stress exposure, and autonomic nervous system dynamics as fundamental contributors to long-term blood pressure control.

The cardiovascular system operates within an integrated neurovisceral network in which emotional processing and cognitive appraisal influence peripheral haemodynamic regulation. Stress-related neural activation directly modulates sympathetic and parasympathetic outflow, thereby shaping vascular tone and cardiac function. Within this systems-based framework, panic disorder offers a particularly informative model for examining how recurrent acute stress responses may influence chronic cardiovascular adaptation.

Panic disorder is characterised by recurrent, unexpected panic attacks accompanied by persistent concern about recurrence and behavioural avoidance. A panic attack involves a rapid surge of intense fear accompanied by pronounced somatic symptoms, including tachycardia, palpitations, dyspnoea, dizziness, trembling, sweating, and acute elevations in blood pressure. From a physiological perspective, these manifestations reflect abrupt activation of the sympathetic nervous system.

Neurobiological models implicate dysregulation within a distributed defensive network involving the amygdala, insular cortex, anterior cingulate cortex, hypothalamus, and periaqueductal grey (Guan & Cao, 2024). The amygdala assigns salience to perceived threats and initiates downstream autonomic mobilisation. The insula integrates interoceptive signals, heightening awareness of bodily sensations. The anterior cingulate cortex contributes to emotional regulation and autonomic control, while the hypothalamus coordinates sympathetic and endocrine responses. Activation of this network triggers sympathetic efferent discharge via brainstem and spinal pathways, producing cardiovascular mobilisation.

Each panic episode therefore constitutes an acute haemodynamic stress event. Blood pressure rises rapidly due to increased cardiac output and systemic vascular resistance. While such responses are adaptive during genuine threat exposure, panic disorder involves repeated activation in the absence of objective danger. Over months and years, recurrent haemodynamic surges may impose cumulative mechanical and biochemical strain on the vascular system.

Epidemiological evidence suggests that panic disorder may be associated with increased hypertension risk. Prospective multinational cohort data demonstrate approximately 1.7-fold elevated lifetime risk of hypertension among individuals with panic disorder independent of demographic and psychiatric covariates (Stein et al., 2014). Cross-sectional investigations reveal consistent comorbidity between panic disorder and elevated blood pressure (Bladowski et al., 2021), while clinical studies report heightened anxiety pathology among individuals with resistant hypertension (Davies et al., 1997). These findings raise the possibility that panic disorder may function not merely as a psychiatric diagnosis but as a potential determinant or amplifier of cardiovascular risk.

The aim of this review is to synthesise epidemiological, autonomic, neurophysiological, endocrine, inflammatory, and psychosocial evidence to evaluate the hypothesis that panic disorder contributes to the development of sustained hypertension.

Methodology

This manuscript constitutes a structured narrative review aimed at synthesising current evidence regarding the relationship between panic disorder and the development of hypertension. A comprehensive literature search was conducted in major biomedical databases, including PubMed, Scopus, and Web of Science, to identify relevant peer-reviewed articles published primarily between 1990 and 2024. Additional references were identified through manual screening of bibliographies of key publications.

Search terms included combinations of the following keywords: “panic disorder,” “panic attacks,” “hypertension,” “blood pressure,” “sympathetic nervous system,” “autonomic dysfunction,” “baroreflex,” “renal sympathetic activity,” “inflammation,” “allostatic load,” and “stress-related cardiovascular disease.” Boolean operators were applied to refine the search strategy and identify studies specifically examining mechanistic or epidemiological associations between panic disorder and cardiovascular outcomes.

Inclusion criteria comprised: (1) human studies investigating panic disorder in relation to blood pressure regulation or hypertension development; (2) prospective cohort studies examining incident hypertension among individuals with anxiety or panic disorders; (3) physiological investigations assessing sympathetic nerve activity, baroreflex function, catecholamine spillover, or neuroendocrine activation; and (4) studies exploring vascular, inflammatory, renal, or metabolic mechanisms potentially linking recurrent stress activation to sustained blood pressure elevation.

Exclusion criteria included case reports without physiological assessment, studies limited exclusively to generalised anxiety disorder without panic-specific analysis, and non-peer-reviewed publications. Animal studies were considered selectively when they provided mechanistic insight relevant to human autonomic regulation.

Given heterogeneity in study design, population characteristics, and outcome measures, a quantitative meta-analysis was not undertaken. Instead, a thematic synthesis approach was adopted. Identified studies were categorised into major domains: epidemiological associations, autonomic nervous system dysregulation, vascular remodeling, renal and endocrine mechanisms, inflammatory and oxidative pathways, metabolic interactions, and psychosocial determinants. This integrative approach allowed for the development of a multilevel conceptual framework linking recurrent panic-related autonomic activation with potential long-term cardiovascular adaptation.

The review aimed not only to summarise existing findings but also to critically interpret mechanistic pathways and identify areas requiring further longitudinal and interventional investigation.

Results

Epidemiological Associations

Prospective data provide the strongest evidence for a temporal association between panic disorder and hypertension. Stein et al. (2014) demonstrated that individuals diagnosed with panic disorder exhibited approximately 1.7-fold increased lifetime risk of developing hypertension compared with those without panic disorder. This association remained statistically significant after adjustment for sociodemographic factors and comorbid psychiatric conditions, suggesting independent contribution.

Cross-sectional analyses further support this relationship. Bladowski et al. (2021) identified consistent comorbidity between panic disorder and elevated blood pressure across community and clinical populations. Although cross-sectional data cannot determine directionality, reproducibility across diverse samples strengthens plausibility.

Clinical case–control research also reveals elevated anxiety disorders among patients with resistant hypertension (Davies et al., 1997), implying potential interaction between psychological dysregulation and treatment-resistant blood pressure elevation.

Autonomic Nervous System Dysregulation

Microneurographic investigations demonstrate enhanced sympathetic baroreflex gain in individuals with panic disorder (Lambert et al., 2002). The baroreflex normally buffers acute fluctuations in arterial pressure through reciprocal modulation of sympathetic and parasympathetic activity. Enhanced gain suggests exaggerated sympathetic responsiveness to haemodynamic changes, potentially contributing to instability in blood pressure regulation.

Single-unit recordings further reveal that sympathetic firing pattern significantly influences catecholamine release (Lambert et al., 2011). Multi-spike firing within a cardiac cycle produces greater noradrenaline spillover than single-spike bursts. Macefield and Wallin (2018) confirmed that altered firing probability amplifies effector responses at vascular and cardiac targets. These findings indicate qualitative dysregulation of sympathetic output in panic disorder.

Chronic catecholamine exposure promotes vascular smooth muscle hypertrophy, arterial stiffness, and impaired endothelial nitric oxide signalling (Esler, 2008b). Recurrent panic-related sympathetic surges may therefore contribute to progressive vascular remodelling beyond transient pressure elevations.

Vascular Remodeling and Endothelial Dysfunction

While transient elevations in blood pressure during panic attacks may appear clinically benign, the cumulative mechanical stress imposed on arterial walls warrants careful consideration. Arterial tissue is biologically dynamic and responds adaptively to repeated haemodynamic strain. Each episode of elevated systolic pressure increases circumferential wall stress, stimulating vascular smooth muscle cell hypertrophy and extracellular matrix remodeling. Over time, these adaptive responses may reduce arterial compliance and increase baseline systemic vascular resistance.

Repeated sympathetic activation contributes directly to these processes. Noradrenaline binding to alpha-adrenergic receptors promotes vasoconstriction but also stimulates smooth muscle proliferation and structural remodeling when chronically elevated. Experimental and clinical evidence demonstrates that chronic sympathetic overactivity is associated with increased arterial stiffness, reduced compliance, and vascular hypertrophy (Esler, 2008b). Panic disorder, characterized by recurrent sympathetic surges, may therefore provide a mechanism for accelerated vascular aging.

Endothelial function represents a critical determinant of long-term blood pressure regulation. The endothelium modulates vascular tone through nitric oxide production, prostacyclin release, and regulation of inflammatory mediators. Acute haemodynamic stress and catecholamine exposure may impair nitric oxide bioavailability, promoting endothelial dysfunction. Recurrent panic-related hypertensive spikes may generate oxidative stress within endothelial cells, reducing vasodilatory capacity and facilitating vasoconstrictive dominance.

Over time, impaired endothelial signaling may shift the vascular system toward a higher resting resistance state. Even modest reductions in nitric oxide availability can meaningfully alter systemic vascular tone. Thus, episodic panic-induced stress may contribute cumulatively to sustained hypertensive physiology.

Blood Pressure Variability and Hemodynamic Instability

Beyond mean blood pressure levels, variability itself has emerged as an independent cardiovascular risk marker. Elevated short-term blood pressure variability is associated with increased risk of stroke, left ventricular hypertrophy, and endothelial injury. Panic attacks introduce abrupt and unpredictable hypertensive surges, thereby increasing short-term variability independent of baseline pressure.

Enhanced sympathetic baroreflex gain observed in panic disorder (Lambert et al., 2002) suggests altered feedback regulation. Rather than efficiently dampening fluctuations, exaggerated sympathetic responses may amplify oscillatory instability. Recurrent episodes of hemodynamic instability may gradually recalibrate baroreflex operating points, shifting resting blood pressure upward.

Paroxysmal hypertension provides a clinically relevant comparison. Pickering and Clemow (2008) described episodic hypertensive crises triggered by psychological stress in individuals without sustained hypertension. Some patients exhibiting repeated paroxysmal episodes subsequently developed chronic hypertension, suggesting a continuum between episodic stress-induced surges and sustained elevation. Panic disorder may represent a similar trajectory.

Neuroendocrine and Hypothalamic–Pituitary–Adrenal Axis Activation

The stress response involves not only sympathetic activation but also neuroendocrine modulation. The hypothalamic–pituitary–adrenal (HPA) axis plays a central role in stress adaptation through glucocorticoid release. Cortisol influences vascular reactivity, sodium retention, glucose metabolism, and inflammatory signaling.

Repeated panic episodes may provoke recurrent HPA activation. Although cortisol dynamics in panic disorder demonstrate variability across studies, anticipatory anxiety and chronic hypervigilance may maintain altered stress hormone regulation. Glucocorticoids potentiate vasoconstrictive responses and influence renin–angiotensin system activity. Chronic dysregulation of these pathways may contribute indirectly to hypertension development.

Esler (2008a) proposed that chronic mental stress represents a biological contributor to essential hypertension. Panic disorder, characterized by repeated acute stress episodes layered upon persistent anticipatory anxiety, may exemplify this model.

Renal Sympathetic Mechanisms

Long-term blood pressure regulation is intimately linked to renal sodium handling. Sympathetic innervation of the kidneys influences renin release, sodium reabsorption, and renal vascular resistance. Recurrent sympathetic activation may transiently increase renin secretion and sodium retention.

Although panic attacks are episodic, repeated renal sympathetic stimulation over extended periods may induce subtle shifts in sodium balance. Even small cumulative changes in sodium handling can meaningfully influence long-term arterial pressure. While direct renal measurements in panic disorder populations remain limited, extrapolation from sympathetic physiology suggests plausible renal contributions.

Inflammatory and Immune Pathways

Chronic psychological stress has been associated with elevated inflammatory markers, including cytokines and C-reactive protein. Inflammation contributes to endothelial dysfunction, vascular stiffening, and atherosclerotic progression. Sympathetic activation influences immune cell trafficking and cytokine production.

Although specific inflammatory profiles in panic disorder require further study, the repeated stress exposure inherent in the disorder may activate immune pathways contributing to vascular pathology. Low-grade chronic inflammation may impair endothelial function and amplify vasoconstrictive responses.

Oxidative stress represents an additional mediator linking sympathetic activation and vascular dysfunction. Catecholamine metabolism generates reactive oxygen species, which may reduce nitric oxide bioavailability and damage endothelial cells. Over time, oxidative stress may contribute to structural vascular remodeling.

Metabolic and Behavioral Interactions

Panic disorder frequently coexists with sleep disturbance, reduced physical activity, and maladaptive coping behaviors. Sleep deprivation increases sympathetic tone and impairs glucose metabolism. Physical inactivity reduces endothelial shear stress, limiting nitric oxide production. Tobacco and alcohol use further increase cardiovascular risk.

While epidemiological analyses often adjust for lifestyle factors, residual behavioral confounding cannot be excluded. However, even when behavioral variables are controlled, associations between panic disorder and hypertension persist (Stein et al., 2014), suggesting that biological mechanisms likely play a substantial role.

Social Determinants and Environmental Stress

Panic disorder prevalence is influenced by trauma exposure, socioeconomic adversity, and chronic environmental stress. These social determinants also correlate with increased hypertension risk. Chronic socioeconomic strain may maintain elevated baseline sympathetic tone, reduce access to preventive healthcare, and increase exposure to unhealthy environments.

Therefore, the relationship between panic disorder and hypertension must be interpreted within a biopsychosocial context. Biological vulnerability interacts with cognitive amplification, behavioral adaptation, and social environment.

Advanced Neurobiological and Multisystem Integration

Emerging evidence suggests that panic disorder may involve persistent alterations within the central autonomic network, extending beyond episodic sympathetic activation. Dysregulation of limbic–brainstem circuitry, particularly involving the amygdala, insula, and prefrontal regulatory regions, may lower the threshold for sympathetic mobilization and reduce autonomic flexibility. Sustained sympathetic bias and diminished parasympathetic modulation, reflected in reduced heart rate variability, may contribute to chronic shifts in cardiovascular regulation.

Repeated sympathetic activation may influence not only acute hemodynamic responses but also long-term regulatory mechanisms. Enhanced renal sympathetic stimulation may intermittently activate the renin–angiotensin–aldosterone system (RAAS), promoting sodium retention and vasoconstriction. Although individual panic episodes are transient, cumulative RAAS activation may contribute to gradual elevation of arterial pressure.

Oxidative stress and endothelial dysfunction represent additional pathways linking recurrent autonomic activation with vascular pathology. Catecholamine-mediated generation of reactive oxygen species may reduce nitric oxide bioavailability, impair endothelial signaling, and promote vascular stiffening. Low-grade inflammatory activation associated with chronic stress exposure may further alter vascular compliance and reinforce sympathetic–immune interactions.

Metabolic factors may amplify these processes. Stress-related glucocorticoid effects on glucose regulation and insulin sensitivity may interact with autonomic imbalance, creating overlapping cardiometabolic risk pathways. Developmental, genetic, and socioeconomic factors may further modulate individual susceptibility.

Collectively, these interacting mechanisms are consistent with the concept of cumulative allostatic load, whereby repeated stress responses impose progressive physiological burden across neural, autonomic, vascular, renal, immune, and metabolic systems.

Taken together, the evidence synthesised across epidemiological, autonomic, neurobiological, renal, inflammatory, and metabolic domains indicates that panic disorder is associated with multiple physiological processes implicated in blood pressure regulation. Although individual mechanisms have been examined separately across studies, their convergence suggests a broader systems-level interaction rather than isolated pathways. The following discussion interprets these findings within an integrative biopsychosocial framework and considers their clinical and preventive implications.

Discussion

The synthesis of epidemiological, autonomic, neurobiological, renal, inflammatory, metabolic, behavioral, and social evidence suggests that the association between panic disorder and hypertension should not be interpreted as incidental comorbidity. Rather, panic disorder may function as a systemic stress-amplifying condition capable of influencing long-term cardiovascular regulation through interacting biological and psychosocial pathways.

At the neurobiological level, dysregulation within the central fear network appears to lower the threshold for autonomic activation. The amygdala–insula–hypothalamic circuitry implicated in panic disorder mediates rapid sympathetic mobilization in response to perceived threat (Guan & Cao, 2024). In affected individuals, benign interoceptive sensations may be catastrophically misinterpreted as life-threatening events, triggering disproportionate autonomic discharge. Recurrent activation reinforces neural pathways through fear conditioning and neuroplastic adaptation, potentially recalibrating baseline autonomic tone.

Autonomic dysregulation represents one of the most compelling mechanistic links to hypertension. Enhanced sympathetic baroreflex gain observed in panic disorder (Lambert et al., 2002) suggests instability in feedback regulation. Rather than buffering blood pressure oscillations, dysregulated baroreflex responses may amplify hemodynamic variability. Elevated blood pressure variability is independently associated with

endothelial dysfunction and cardiovascular risk. Repeated panic-induced hypertensive spikes may therefore exert structural effects on vascular tissue beyond transient fluctuations.

Multi-spike firing patterns amplify catecholamine spillover (Lambert et al., 2011; Macefield & Wallin, 2018), intensifying vascular exposure to noradrenaline. Chronic catecholaminergic stimulation promotes smooth muscle hypertrophy, increased extracellular matrix deposition, and arterial stiffness (Esler, 2008b). These structural adaptations elevate systemic vascular resistance and contribute directly to sustained hypertension.

From a vascular standpoint, repeated exposure to elevated systolic pressures increases cyclic strain on arterial walls. Mechanical stress stimulates remodeling processes that gradually reduce arterial compliance. As arteries stiffen, baroreceptor sensitivity decreases, impairing feedback inhibition of sympathetic outflow. This impairment may lead to higher resting sympathetic tone, creating a feed-forward cycle in which structural vascular changes reinforce autonomic dysregulation.

The renal dimension further integrates autonomic and vascular mechanisms. Intermittent sympathetic stimulation of renal pathways may promote episodic renin release and sodium retention. Although each episode is brief, cumulative renal adjustments over time may contribute to incremental upward shifts in arterial pressure set points. Activation of the renin–angiotensin–aldosterone system also exerts pro-inflammatory and pro-fibrotic effects within vascular tissue, linking renal activation to structural remodeling.

Inflammatory and oxidative stress pathways may serve as bridging mechanisms between psychological stress and vascular pathology. Recurrent stress responses can activate inflammatory cascades even in the absence of infection. Low-grade chronic inflammation contributes to endothelial dysfunction and arterial stiffness. Catecholamine metabolism generates reactive oxygen species, reducing nitric oxide bioavailability and impairing vasodilatory capacity. Together, these processes create a microenvironment conducive to hypertensive progression.

The endocrine component adds additional complexity. Recurrent hypothalamic–pituitary–adrenal axis activation may influence vascular reactivity and metabolic regulation. Glucocorticoid fluctuations alter insulin sensitivity and may contribute to cardiometabolic risk profiles. While cortisol dynamics in panic disorder require further clarification, chronic anticipatory anxiety may maintain subtle endocrine dysregulation that interacts with autonomic imbalance.

Importantly, these biological mechanisms operate within a broader biopsychosocial framework. Cognitive amplification of bodily sensations, avoidance behaviors, sleep disturbance, and maladaptive coping strategies may compound physiological vulnerability. Reduced physical activity limits endothelial shear stress that normally promotes nitric oxide production. Substance use may independently increase cardiovascular risk. Social determinants, including trauma exposure and socioeconomic adversity, may sustain chronic stress activation and limit access to preventive care.

It is essential to acknowledge that panic disorder does not deterministically lead to hypertension. Individual resilience factors—including adaptive coping strategies, early treatment, social support, and lifestyle modification—may mitigate risk. Identifying protective mechanisms represents an important future research priority.

Importantly, the directionality of the relationship between panic disorder and hypertension may not be exclusively unidirectional. Emerging evidence suggests that sustained hypertension itself may contribute to heightened anxiety symptoms through increased interoceptive awareness of cardiovascular sensations. Elevated blood pressure, vascular pulsatility, and cardiac hypercontractility may enhance perception of bodily signals, which in vulnerable individuals could trigger anxiety amplification and panic-related cognitive interpretations. Thus, a bidirectional feedback model in which hypertension and panic disorder mutually reinforce one another warrants further empirical investigation.

Methodologically, existing research demonstrates both strengths and limitations. Prospective cohort evidence linking panic disorder to incident hypertension provides temporal support, yet causality remains unproven. Reverse causality and shared vulnerability factors may partially account for the observed associations. Physiological investigations utilizing microneurography offer mechanistic insight but are often limited by small sample sizes. Heterogeneity in panic severity, medication exposure, and comorbid psychiatric conditions introduces variability. Future studies should incorporate multimodal longitudinal designs combining ambulatory blood pressure monitoring, heart rate variability assessment, inflammatory biomarkers, renal function evaluation, and neuroimaging.

Interventional research is particularly important. If effective treatment of panic disorder attenuates sympathetic hyperactivation and reduces long-term blood pressure risk, this would provide stronger evidence

for causality. Randomized controlled trials incorporating cardiovascular outcomes as secondary endpoints could clarify whether modifying psychological stress responses alters hypertensive trajectories.

Clinically, recognition of panic disorder as a potential cardiovascular risk amplifier carries significant implications. Screening for anxiety symptoms in patients with labile or resistant hypertension may facilitate early identification of contributory psychological factors. Conversely, routine blood pressure monitoring in patients with chronic panic disorder may enable early detection of emerging hypertensive trends. Integrated care models bridging psychiatry and cardiology may enhance preventive strategies.

At the population level, the intersection of panic disorder and hypertension underscores the necessity of interdisciplinary public health approaches. Both conditions are highly prevalent globally. Even modest risk amplification associated with panic disorder may translate into substantial disease burden. Public health initiatives promoting stress resilience, early mental health intervention, and reduction of socioeconomic stressors may yield downstream cardiovascular benefits.

Ultimately, the relationship between panic disorder and hypertension reflects the interconnected nature of neural circuitry, autonomic regulation, vascular biology, endocrine modulation, immune activation, behavior, and social context. Systems-based medicine that acknowledges these interactions may provide a more comprehensive framework for understanding and preventing chronic cardiovascular disease.

Systems-Level Interpretation

The long-term interaction between panic disorder and hypertension is best conceptualised as a process of cumulative cardiovascular adaptation to recurrent neural stress activation. Rather than viewing panic attacks as isolated autonomic events, it is more appropriate to consider their repeated occurrence as a source of progressive physiological recalibration.

Recurrent sympathetic surges may contribute to vascular remodeling, arterial stiffening, and altered baroreflex sensitivity, gradually shifting baseline hemodynamic regulation. Intermittent renal sympathetic activation and metabolic stress responses may further reinforce subtle upward drift in arterial pressure over time. Even modest but persistent sympathetic bias between panic episodes may exert cumulative cardiovascular influence.

These mechanisms do not operate in isolation. Developmental vulnerability, genetic predisposition, sex-related hormonal modulation, sleep disturbance, and socioeconomic stress may all modify individual trajectories. The relationship between panic disorder and hypertension therefore likely reflects multilevel interaction within interconnected regulatory systems rather than a single linear pathway.

Importantly, this framework also supports the possibility of bidirectional reinforcement, whereby early vascular changes and heightened interoceptive awareness may amplify anxiety symptoms, further sustaining autonomic activation.

Clinically, early identification and effective treatment of panic disorder may reduce cumulative sympathetic burden and potentially attenuate long-term cardiovascular risk. Future longitudinal and multimodal research is required to clarify causal pathways and determine whether targeted psychological and autonomic interventions influence hypertensive trajectories.

Limitations

Several limitations should be acknowledged when interpreting the findings synthesised in this review. First, a substantial proportion of the available evidence derives from observational and cross-sectional studies. Although prospective cohort investigations suggest a temporal association between panic disorder and subsequent hypertension development, causal inference remains limited. Residual confounding related to lifestyle factors, medication use, socioeconomic status, and comorbid psychiatric conditions cannot be entirely excluded.

Second, mechanistic studies examining autonomic dysfunction, sympathetic nerve activity, and baroreflex regulation in panic disorder frequently involve relatively small sample sizes due to the technical complexity of microneurography and related physiological methods. While these investigations provide valuable insight into underlying pathways, limited sample size may reduce generalisability to broader populations.

Third, heterogeneity in diagnostic criteria, severity of panic disorder, duration of illness, and treatment status across studies complicates direct comparison of findings. Pharmacological interventions commonly used in panic disorder, including selective serotonin reuptake inhibitors and other psychotropic agents, may independently influence autonomic balance and cardiovascular function. Few studies adequately stratify participants according to treatment exposure.

Fourth, the majority of studies focus on peripheral cardiovascular parameters, while fewer investigations integrate multimodal assessment incorporating neuroimaging, inflammatory biomarkers, renal function, and longitudinal ambulatory blood pressure monitoring. Consequently, the proposed multilevel model remains partially theoretical and requires further empirical validation.

Finally, publication bias cannot be excluded, as studies demonstrating significant associations between psychological stress and cardiovascular outcomes may be more likely to be published than null findings.

Despite these limitations, the convergence of epidemiological, physiological, and mechanistic evidence supports the plausibility of a meaningful association between recurrent panic-related autonomic activation and long-term blood pressure regulation. Future longitudinal and interventional studies are required to clarify causal pathways and quantify the magnitude of risk.

Conclusions

The cumulative evidence synthesized across epidemiological, autonomic, neurobiological, renal, inflammatory, metabolic, behavioral, and social domains supports the hypothesis that panic disorder may function as a cardiovascular risk amplifier.

While causality remains to be definitively established, the convergence of findings underscores the importance of integrating mental health assessment within cardiovascular prevention frameworks. Systems-based medicine that acknowledges the interconnected nature of psychological stress and cardiovascular physiology may ultimately contribute to more comprehensive strategies for reducing global hypertension burden.

Recognizing panic disorder not solely as a psychiatric condition but as a potential systemic stress-related disorder with cardiovascular implications represents a critical step toward interdisciplinary prevention and treatment approaches.

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Research concept and design – Iga Kwiecień, Karolina Bartoszewska, Julia Głowacz, Julia Ługowska, Weronika Matwiejuk, Anna Nagrodzka.

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Critical review of the article – Iga Kwiecień, Karol Marcyś, Jakub Komorowski – Roszkiewicz.

Supervision, project administration – Iga Kwiecień.

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