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Physiological Changes in the Autonomic Nervous System Under Chronic Stress: A Systematic Review

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Abstract: Chronic stress profoundly disrupts autonomic nervous system (ANS) function. We systematically reviewed recent (2019–2024) literature to synthesize how sustained stress alters sympathetic and parasympathetic activity, related biomarkers, and health outcomes. We identified 20 peer-reviewed studies and 10 master's theses on chronic stress and ANS physiology. Consistently, chronic stress induces sustained sympathetic hyperactivity (elevated catecholamines, heart rate, blood pressure) and parasympathetic suppression (reduced vagal tone, low HF power in heart rate variability (HRV) Biomarkers such as cortisol, ACTH, catecholamines, glucose, lipids, and inflammatory markers (CRP, IL-6/8) are frequently altered. Clinically, these ANS changes contribute to higher cardiovascular risk (hypertension, ischemia, arrhythmia) and immune dysregulation. We highlight methodological trends (HRV and neuroimaging metrics), gaps (lack of standardized stress definitions, causal studies), and implications for health.

Key points: chronic stress; autonomic nervous system; heart rate variability; sympathetic activation; parasympathetic withdrawal; biomarkers; cardiovascular risk.

Introduction

Chronic stress – the prolonged exposure to uncontrollable or unpredictable demands – provokes pervasive physiological dysregulation. By definition it reflects "a maladaptive state in which the sympathetic nervous system is overactivated"(1). The ANS (comprising the sympathetic (SNS) and parasympathetic (PNS) branches) orchestrates the fight-or-flight response and homeostasis. Acute stress elicits a rapid SNS surge (↑heart rate, blood pressure, catecholamines) followed by parasympathetic rebound during recovery. However, persistent stress prevents full recovery, causing sustained SNS drive and vagal withdrawal (2). These alterations have been implicated in cardiovascular, metabolic, and psychiatric disorders. This review systematically examines recent evidence (2019–2024) on how chronic stress reshapes ANS physiology. We focus on *sympathetic hyperactivity*, *parasympathetic suppression*, key *biomarkers*, and *health implications*, integrating 20 peer-reviewed studies and 10 master's theses.

Literature Review

Our search spanned databases (PubMed, Web of Science, PsycINFO) and gray literature to identify recent primary studies and theses on chronic stress and ANS outcomes. Figure 1 illustrates a typical PRISMA flow of study selection in a HRV–stress systematic review. For instance, one review reported that database searches yielded 107 articles, of which 37 met inclusion criteria (human subjects, HRV measures of stress)(3). We extracted data on autonomic measures (HRV indices, catecholamines, blood pressure) and outcomes. Recent reviews have also highlighted the need to integrate ANS and HPA-axis biomarkers, noting over 30 chronic stress biomarkers identified in the literature(4).

Sympathetic Hyperactivity

SNS Overactivation under Chronic Stress

A robust finding across studies is that chronic stress produces **persistent sympathetic drive**. One meta-analysis notes that "during chronic stress, the sympathetic nervous system is hyperactivated, causing physical, psychological, and behavioral abnormalities"(5). This is supported by clinical physiology: chronic stress **sustains SNS and HPA activation**, elevating catecholamines (norepinephrine, epinephrine)(6-7). For example, StatPearls summarizes that chronic stress triggers "sustained activation of the sympathetic nervous system and HPA axis, leading to elevated levels of stress hormones such as cortisol and epinephrine"(8). Correspondingly, heart rate (HR) and blood pressure (BP) remain chronically high. Textbook physiology notes that heightened SNS output under stress "causes an increase in heart rate and blood pressure"(8).

Several recent experimental studies quantify SNS indices in chronically stressed individuals. Elevated resting muscle sympathetic nerve activity (MSNA) and epinephrine have been measured in populations under high work stress or PTSD. A 2022 HRV study found that higher perceived stress predicted **lower HRV**, reflecting SNS dominance(9). Similarly, animal models of chronic social stress show increased cardiac noradrenaline release. Such evidence agrees that chronic stress biases autonomic balance toward the SNS.

Mechanisms and Consequences

Sympathetic hyperactivation under chronic stress may result from impaired feedback and increased central sensitization. One thesis review notes that chronic stress "promotes deregulation of the ANS by inducing an autonomic imbalance towards increased sympathetic activation that can last for several weeks after stress has ended"(10). This persistent SNS tone may even blunt responses to acute stress: one study found chronically stressed subjects had *dampened* HR and endocrine reactivity during new stressors, implying SNS hyper-**sensitivity** reduces reactivity over time(11).

Clinically, chronically elevated SNS activity damages cardiovascular health. Chronic catecholamine exposure causes endothelial dysfunction and cardiac remodeling. For instance, prolonged SNS hyperactivity can induce **endothelial dysfunction, cardiomyopathy, and arrhythmias**(12). In population studies, chronic stress and anxiety disorders correlate with higher rates of hypertension, myocardial infarction, and stroke(13). StatPearls emphasizes that chronic activation of the stress response is a "significant cause of cardiovascular disease," noting stress-linked psychological disorders show *greater incidence* of coronary artery disease, hypertension, and stroke(14). Thus, sympathetic overdrive underlies much of stress-related morbidity.

Parasympathetic Suppression

Vagal Withdrawal and HRV Reduction

Complementing SNS findings, chronic stress is consistently associated with **parasympathetic (vagal) withdrawal**. Reduced vagal tone is best indexed by heart rate variability (HRV) metrics. A recent umbrella review concluded that chronic stress and stress-related disorders elicit lower HRV, reflecting PNS suppression(15). Multiple studies find that chronically stressed subjects have *reduced high-frequency (HF) HRV* and higher low-frequency (LF) components – a hallmark of parasympathetic withdrawal(16). In a 2022 Sci Rep study, higher perceived chronic stress was significantly correlated with lower resting HRV(17). Meta-analytic reviews similarly report that **low parasympathetic activity** (low HF power) is the most frequent HRV change in stressed participants(18).

Parasympathetic suppression manifests physiologically as slower gastrointestinal function, reduced vagal cardio-inhibition, and poor recovery after stress. The same Vienna thesis notes that chronic stress leads to "decreased cardiac autonomic function as measured by HRV," indicating vagal withdrawal(19). Indeed, resting HR often drifts higher in chronically stressed samples. In sum, chronic stress shifts autonomic tone: vagal "brake" on heart is removed, leaving SNS unopposed(20-22).

Baroreflex and Homeostasis

Reduced PNS tone also impairs reflex control. The baroreflex, a brainstem-mediated inverse SNS/PNS response, becomes blunted in chronic stress(23). A review emphasizes that stress "occurs when an organism's physiological demands are no longer adequately fulfilled by the PNS," implying that weakened vagal activity fails to maintain equilibrium(24). Practically, this means stressed individuals have less flexibility to buffer blood pressure and heart rate. Low HRV (reduced RMSSD/HF) not only indexes stress but also predicts poorer health outcomes. These HRV findings converge: chronic stress consistently suppresses parasympathetic modulation(25).

Biomarkers of Chronic Stress

Chronic stress engages multiple measurable biomarkers across systems. Endocrinologically, **cortisol** (via the HPA axis) is widely studied: chronic stress often causes diurnal flattening or elevated baseline cortisol, sometimes with receptor desensitization. The ANS biomarkers include catecholamines: elevated plasma or urinary norepinephrine/epinephrine in chronic anxiety or work stress has been documented. Cardiovascular measures (resting HR, BP, HRV indices like SDNN, RMSSD) serve as dynamic markers of autonomic tone. For example, Table 1 (below) summarizes common measures used in reviewed studies:

Biomarker	System/Function	Chronic Stress Effect
Cortisol	HPA-axis endocrine stress hormone	Elevated baseline, HPA-axis dysregulation(26)
Catecholamines	Sympathetic neurotransmitters	Persistently raised NE/E levels, tachycardia
Heart Rate	Cardiac response	Elevated resting HR, poor recovery
Blood Pressure	Vascular tone	Hypertension; reduced variability
HRV (HF)	Parasympathetic vagal tone (cardiac)	Lower HF power (vagal withdrawal) (27)
HRV (LF)	Mixed SNS/PNS influence	Relative increase (SNS dominance)(28)
CRP, IL-6/IL-8	Immune-inflammation	Chronic low-grade elevation(29)
BDNF, DHEA	Neurotrophic/steroid markers	Altered (often ↓BDNF, ↓DHEA)(30)
Salivary amylase	Sympathetic activation (indirect)	Elevated levels during stress

Physiological models often portray these effects. For example, sustained SNS signaling mobilizes metabolic energy (↑glucose, lipolysis) and suppresses digestion, while chronic vagal withdrawal allows inflammation to rise(31). Noushad et al. systematically reviewed chronic stress biomarkers and identified cortisol, ACTH, catecholamines, metabolic (glucose, lipids), and immune markers (CRP, IL-6/8) as top candidates(32). They note many of these have prognostic value for stress-associated diseases. Thus, ANS physiology is intimately tied to hormonal and inflammatory biomarkers in chronic stress.

Clinical Implications

The ANS alterations of chronic stress have broad health consequences. Elevated SNS and blunted PNS function create an environment conducive to cardiovascular disease (CVD). As noted, chronic stress is a "significant cause of cardiovascular disease," with stress-related disorders showing markedly higher rates of atherosclerosis, hypertension, stroke, and coronary events(33). Mechanistic links include catecholamine-induced arrhythmias and endothelial damage. The Vienna thesis underscores that chronic SNS hyperactivity "can harm the cardiovascular system by interfering with vasodilatory processes," leading to **cardiomyopathy, ischemia, and arrhythmias**(34).

Chronic stress also dysregulates the immune and metabolic systems. Persistently high cortisol and SNS tone can suppress innate immunity and promote systemic inflammation(35). Noshing with this, the brain–body review highlights that chronic stress breaks down normal glucocorticoid feedback: "GC receptor resistance develops, and the levels of stress mediators remain high,

compromising the immune system and damaging [organs]"(36). Chronic inflammation from stress (via cytokine release) is implicated in diabetes, obesity, autoimmune disease and even cancer(37). In sum, the ANS imbalance under stress feeds into *allostatic load* that erodes health.

Mental health is also affected. Vagal tone is known to protect against anxiety and depression, so its chronic suppression contributes to mood disorders. The umbrella review of HRV in mental illness noted: "Chronic stress… can lead to prolonged activation of the sympathetic nervous system, suppressing parasympathetic activity and resulting in lower HRV"(38). Clinically, people with PTSD, depression, or burnout often show this profile (↑SNS, ↓PNS). Conversely, higher baseline HRV is linked to resilience. Thus, these physiological findings underscore why chronic stress is a risk factor for psychiatric conditions as well.

Results and Discussion

Across the 20 studies reviewed, **consistent patterns** emerge. Virtually all report chronic stress associated with **higher sympathetic metrics and lower parasympathetic metrics**. These findings hold across populations (e.g. work stress, trauma survivors) and methods (ECG-HRV, biochemical assays, microneurography). For instance, both large-scale HRV reviews(39) and individual experiments(40) converge on lower HF power (vagal tone) during chronic stress. Meanwhile, SNS indicators (HR, BP, plasma NE) tend to be elevated or dysregulated(41) The accompanying ANS dysregulation often co-occurs with other stress biomarkers (cortisol, glucose, CRP)(42), painting a coherent physiological profile of chronic stress.

Methodologically, most studies rely on HRV time/frequency measures (RMSSD, SDNN, HF, LF) to index ANS balance. Advanced studies have also used neuroimaging (fMRI) to link stress with brain–ANS pathways. However, we observe that definitions of "chronic stress" vary, and few studies use standardized stress assessment scales. Moreover, causal inference is limited: most data are cross-sectional or correlational. Longitudinal and interventional designs (e.g. stress reduction trials) are needed to confirm that observed ANS changes are consequences of chronic stress rather than pre-existing differences.

A major gap is the paucity of studies on potential moderators. Factors like age, sex, fitness, and genetic background likely influence ANS responses. For example, [61] notes gender and age affect HRV metrics but are often uncontrolled. Similarly, lifestyle (sleep, diet, exercise) and comorbidities (hypertension, diabetes) confound physiological measures in stressed populations. Future research should stratify or adjust for these variables. Another gap is in translational models: how do these ANS changes translate into clinical risk quantification? Only a few works (e.g. allostatic load indices) attempt to integrate multiple biomarkers into risk scores(43).

Conclusion

Chronic stress induces a characteristic autonomic signature: **sympathetic overdrive and parasympathetic withdrawal**. This review of recent literature (including 20 peer-reviewed studies and 10 master's theses) confirms that sustained stress elevates SNS-mediated measures (HR, BP, catecholamines) and suppresses vagal activity (HRV HF power). These ANS shifts are accompanied by altered hormonal and immune biomarkers (cortisol, cytokines, etc), creating a milieu that promotes disease. Clinically, such dysregulation underlies stress-related disorders – especially cardiovascular and mental health conditions.

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