The Role of Chronic Stress in the Pathophysiology of Metabolic and Cardiovascular Disease

By

Shruthi Nandakumar

Agard Research Associates Inc.
Agard Research Associates Inc. - Research Division
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Introduction

Chronic psychological stress is a mental issue that causes significant physical harm. Ideally, the effects of stress are meant to adapt one's body to fight against perceived stress. However, chronic stress is an extreme result of these adaptive mechanisms that cause major physiological issues. These effects are seen via the effects of cortisol, a steroid hormone produced via the hypothalamic-pituitary-adrenal axis as well as inflammation as a response to stress. It has a considerable influence on metabolism, the immune system, and cardiovascular system due to its effects on blood glucose concentration and other vital processes.[1] Type 2 Diabetes Mellitus (T2DM), hypertension, and obesity are metabolic disorders with increasing global prevalence. T2DM is a chronic disease arising from the development of insulin resistance, leading to high blood glucose concentrations. This may cause further complications if left untreated, including damage to the eyes, renal damage, neuropathy, and heart damage.[2] Obesity is an excessive accumulation of fat posing a risk to health. Complications include diabetes, as well as musculoskeletal issues like osteoarthritis, as well as some cancers.[3] Hypertension is also a chronic condition in which measured blood pressure is over 130 mmHg systolic and/or over 80 mmHg diastolic. This disease further increases the likelihood of other complications in the body, including heart attacks, strokes, heart failure, renal issues, vision problems, and atherosclerosis.[4] It is certain that these diseases hold certain controversy, particularly with diet culture and body positivity. Regardless, it is vital to look at these diseases from a clinical standpoint under the lens of stress and how its effects may exacerbate or cause them.

This review serves to explore how chronic stress affects chronic disease by incorporating recent evidence examining cortisol as a predictor or biomarker of T2DM, hypertension, obesity. We explore stress's mechanism and role in these diseases, as well as further racial and ethnic disparities in stress patterns and metabolic diseases, and the potential confounding presence of stress-related eating behavior.

A systematic literature review was conducted using Google Scholar, as well as institutional research databases for peer-reviewed articles published after 2010. The inclusion criteria were the search terms 'diabetes', 'cortisol', 'hypercortisolism', 'obesity,' 'hypertension,' 'metabolic syndrome,' and similar terms. Studies consulted were clinical in nature, with preference towards government organizations and academic institutions.

Thesis

Chronic psychological stress exerts a clinically significant influence metabolically, resulting in chronic disease through sustained activation of neuroendocrine and inflammatory pathways. Although acute stress responses are adaptive, persistent activation of the hypothalamic-pituitary-adrenal axis and sympathetic nervous system results in cortisol dysregulation, chronic inflammation and further disease due to maladaptive behavioral responses. These issues directly contribute to the development of type 2 diabetes mellitus, obesity, and hypertension. Recent evidence supports cortisol not only as a mediator, but also as a biomarker for stress related disease, with effects on insulin resistance, visceral adiposity, and increased blood pressure. Furthermore, stress related eating behaviors as well as racial and ethnic disparities may amplify these physiological mechanisms, increasing disease risk in these populations. Understanding chronic stress as a direct, controllable aspect in chronic disease is essential in the treatment and mitigation of type 2 diabetes mellitus, obesity, and hypertension.

Diabetes & Obesity

T2DM is marked by insulin resistance, which in turn oversees increased HbA1C, increased triglycerides, and lower HDL ("good" cholesterol). All these are a result of hypothalamic-pituitary-adrenal (HPA) axis activation, autonomic nervous system (ANS) activation, and inflammation. HPA axis activation increases cortisol and by effect, increases intra-abdominal fat, causes insulin resistance, and causes T2DM. This direct relationship of cortisol with insulin resistance and intra-abdominal fat is evidence of the strong relationship between cortisol and diabetes as well as obesity. ANS activation results in increased epinephrine and norepinephrine which directly increases insulin resistance. Inflammation increases the cytokine interleukin-6 which increases C-reactive protein via liver stimulation, which in turn both causes insulin resistance and causes endothelial dysfunction, both causes of T2DM.[5] Another major effect of chronically increased blood glucose levels is damage to mitochondria as well as mitochondrial DNA, which contributes to telomere shortening. T2DM often is comorbid with obesity. In fact, visceral adipose tissue is a source of inflammatory factors that further circulate to the pancreas and affect insulin sensitivity.[6] This is especially concerning as cortisol as a result of chronic stress, favors a higher distribution of white adipose tissue, specifically to the abdominal region. To further increase the feedback loop, it also increases the appetite for '"energy-dense" foods. [8] This acts as an unbreakable cycle that feeds into the loop of stress, obesity, and hyperglycemia. Most interestingly, cortisol responsiveness has been found to act as a metabolic marker for those who are likely to gain weight.[9]

Hypertension

The connection between stress and blood pressure is arguably the most well understood among the general population. Generally, stressful situations cause temporary blood pressure increases. Specifically, in situations where a lot is expected of an individual, but the individual perceives there to be a lack of resources, there is an increase in heart rate and blood pressure. The opposite is true as well; when there are sufficient resources, but the situational demand is still high, there are only smaller increases in blood pressure. In this study, blood pressure via smartphone optic sensor was measured, as well as self-reported emotional, psychosocial and behavioral data. Utilizing a baseline of blood pressure measured during the lowest measured heart rate, the study showed that with increasing perceived stress, both systolic and diastolic blood pressure were significantly higher than the baseline.[10]

Stress perception has significant effects in a neurological sense. Environmental changes are perceived by the brain to be "stressful" via the neocortex or the limbic system (fight or flight responses). A neuroendocrine response to stress will occur if an individual feels fearful or incapable of handling the situation. As such, the sympathetic nervous system and the HPA axis are activated. As such, allostasis occurs, allowing the body to remain stable under environmental changes. [11] Nonetheless, these mechanisms pose a risk if stress is chronic. Increased blood pressure from mental stress has been related to carotid atherosclerosis.[12]

Chronic psychosocial stress (from work, relationships, poverty, discrimination) contributes to hypertension due to repeated sympathetic nervous system activation, and prolonged activation via rumination on stressful situations. Rather than reactivity (the immediate increase of blood pressure), it is suggested that a return to normal blood pressure after the stressful event is more important. Due to the importance of rumination and its prolonged increase in blood pressure, intervening via stress relief methods such as meditation has been shown to significantly reduce blood pressure.[13]

Racial & Ethnic Disparities

When considering at-risk populations, it is certain that stress affects certain people more than others. Overall, individuals that are Asian, Hispanic, and Black see higher levels of reported stress than white individuals. Among these groups, it is certain that stressful events arising from economic, cultural, and societal expectations contribute to their risk. [14] It becomes significant that we see an increased rate of undiagnosed hypertension and diabetes in these populations compared to white individuals. [15] With regards to inflammatory markers, Black and Hispanic individuals were among the highest risk categories for CRP and IL-6 levels. [16]

Stress-Related Diet Changes

Stress eating is a behavior almost everyone can relate to, and poses certain risks to health if uncontrolled. Stress causes a negative mental experience, which in turn causes some to turn to "junk" foods. Stress influences eating behavior as high perceived stress is inversely related to a healthy diet.[17] As seen in the "Reward Based Stress Eating Model" we see that cortisol motivates calorically dense food intake. In fact, both stress and "junk" food stimulate endogenous opioid release and decrease the effects of the HPA axis, which attenuates the stress response. In this way, stress eating becomes compulsive, like an addiction. Certain calorically dense and palatable food may gain "reward" value via cortisol's influence over neuroendocrine and peptide mediators.[18]

Conclusion

The evidence reviewed demonstrates chronic psychological stress is clearly a mechanistic component of type 2 diabetes mellitus, obesity, and hypertension. Prolonged HPA axis and sympathetic nervous system activation directly leads to sustained cortisol exposure, inflammatory signaling, and autonomic imbalance, increasing insulin resistance, visceral fat accumulation, and elevated blood pressure. These physiological effects are further reinforced via stress related eating behaviors, mainly via the rewarding of calorically dense foods, which temporarily mediate stress while perpetuating metabolic dysregulation. Further, disparities in stress exposure and physiology among racial and ethnic minorities highlight the importance of chronic stress as a contributor to disease in certain populations. Chronic stress is a vital aspect when understanding causes of disease. Addressing neuroendocrine regulation, the inflammatory response, behavior and the socioeconomic environment is key in finding effective prevention, management, and treatment strategies going forward.

This review aligns closely with the mission of Agard Research Associates by advancing rigorous, interdisciplinary research that connects empirical evidence to broader questions of public health, institutional responsibility, and societal well-being. By synthesizing clinical and epidemiological evidence on chronic stress, neuroendocrine dysregulation, and metabolic and cardiovascular disease, the analysis reflects the organization's commitment to evidence-based inquiry that informs both professional practice and public understanding. The emphasis on structural stressors, behavioral pathways, and racial and ethnic disparities situates biological mechanisms within real world social and policy contexts, reinforcing Agard Research Associates' focus on research that bridges science, public affairs, and institutional decision making. In doing so, the review contributes to the organization's broader goal of producing accessible scholarship that supports prevention, equity, and informed policy responses to complex health challenges.

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