



PHYSIOLOGICAL ADAPTATIONS TO CHRONIC STRESS: A CLINICAL AND BIOCHEMICAL EVALUATION OF CORTISOL REGULATION AND CARDIOVASCULAR HEALTH IN ADULTS

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Abstract

Largely, chronic psychological stress is being established as a biological mediator of cardiometabolic risk. The problems with hypothalamic-pituitary-adrenal axis dysregulation and autonomic disregulation can be observed in the form of the varying cortisol patterns and unfavorable cardiovascular phenotypes. The current paper compared the endocrine and cardiovascular adaptation to chronic stress in adulthood. This was a cross-sectional analytical study that was carried out in a tertiary research establishment. Those adults aged 25-60 years who had experienced persistent stress [?]6 months were recruited after screening and exclusions. Stress burden was measured by using standardized questionnaires. Sera and salivary samples were taken fast to measure cortisol (diurnal profile) and biochemical (C-reactive protein, lipids) samples. Cardiovascular measures were blood pressure, resting heart rate, heart-rate variability (time- and frequency-domain measures) and carotid-femoral pulse wave velocity. Multivariate regression was used to test the relationship between stress indices, cortisol patterns, and cardiovascular consequences controlling by age, sex, Body Mass Index (BMI), and lifestyle variables. Two hundred and ten subjects (mean age 41.7 $\pm$ 9.3 years; 54.3% female) were studied. There was a flattened diurnal slope of cortisol with high evening levels. The adjusted models showed a positive correlation between serum and evening salivary cortisol and systolic blood pressure, and the lower the vagal indices the stronger the positive association between pulse pressure and vagal indices. There were also signs of mild inflammatory and lipid disturbances on biochemical markers and they are a result of developing cardiometabolic demand. Adults also had

chronic stress that was linked to the dysregulation of Hypothalamic-Pituitary-Adrenal (HPA)-axis, and cardiovascular profiles were unfavorable. An early detection and specific prevention of cardiometabolic risk associated with stress might be achieved by incorporating the measures of diurnal cortisol, Heart Rate Variability (HRV), and vascular stiffness into the regular routine assessment.

Keywords: Chronic stress, cortisol, heart-rate variability, arterial stiffness, cardiometabolic risk.

1. Introduction

Chronic stress is a well-known physiological and clinical issue that affect adult health significantly. It also produces long-term stimulation of neuroendocrine systems that are developed to respond to the short-term survival but are maladaptive when activated continuously. Governing the human stress response, the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system condition give rise to complex biochemical and cardiovascular changes, which determine the morbidity and disease progression throughout life. The growing body of evidence supports the notion that chronic stress not only changes the numerous physiological biomarkers but also changes the cardiometabolic risk, disrupts endocrine cycles, and changes the onset or progression of various chronic diseases such as hypertension, diabetes, and cardiovascular diseases.¹ As exposure to chronic stresses is becoming a widespread occurrence in modern societies, determining how these stresses are embedded physiologically, changes in biochemical signatures, and clinical concerns has emerged as a major health and treatment concern in the community. The neuroendocrine reactivity, energy consumption, and systemic inflammatory reactions interact in a complex manner in physiological adaptation of persistent stress. The sex-specific differences in the long-term exposure to stress that affect the metabolic process and cardiovascular processes may be explained by very different mechanisms: the evolutionary energy-allocation, immune, and hormonal regulation.² The fact that sex differences in biological sexes exist in the long-term exposure to stress also suggests the need to investigate the physiological burden of stress using multiple perspectives that are based on autonomic functioning, endocrine dynamics, and tissue-based biomarkers. Chronic stress also is associated with the biological aspect of allostatic load wherein the repeated induction of stress networks progressively interferes with the control systems needed to assure stability in the body. This cumulative impairment of numerous organ systems is the key to the pathogenesis of cardiovascular diseases, metabolic disruptions, and neurocognitive impairment.^{3,4}

Cortisol is the one of the most important biochemical predictors of chronic stress. Being the final product of HPA axis, cortisol controls the level of glucose metabolism, immunity, blood pressure stability, and cardiovascular response. Cortisol secretion dysregulation, either in terms of a flat diurnal slope, or elevated evening levels or abnormal reactivity, signifies impaired cortisol-mediated processes in physiological adaptation to chronic stress.⁵ Recent works also indicate that cardiovascular responses to chronic stress can be viewed as the other important dimension of physiological adaptation. Exposure to stress over the long term, which promotes atherosclerotic changes, platelet aggregation, systemic inflammatory mediators, and dysfunctional autonomic responses, increases the odds of cardiovascular morbidity, as recent clinical and epidemiological studies demonstrate.¹⁰ Stress has the potential to influence thrombogenic pathways, and thus, increased reactivity of the sympathetic nervous system and altered vascular physiology are also key factors.¹¹ Salivary cortisol levels, levels of α -amylase and heart-rate variability patterns are all subclinical biomarkers that have been shown to be promising predictors of cardiometabolic vulnerability. These biomarkers are highly clinical as they are sensitive and non-invasive, which means that they are useful in identifying the initial signs of dysregulation in the stress-related context. The applicability of cortisol control is also applied to therapeutic and behavioral intervention. There is evidence that there is a role of using selective health interventions (behavioral, psychological, or lifestyle-based) to repair aspects of cortisol regulation and psychosocial functioning in long-term stressed adults.¹² Studies in adolescents and adults further indicate that cortisol, insulin sensitivity,

and inflammatory processes interact to cause metabolic diseases because of long-term stress exposure. In addition, exercise, good as it is in balancing cardiovascular risk, can be a source of stress to the body, both in itself with excessive exercise, and within already strained psychological conditions, making it challenging to the planning of therapies.¹⁴ On a psychobiological perspective, chronic stress can cause the body to respond with stress in almost all major physiological systems: neuroendocrine, cardiovascular, metabolism, and immune systems. These combined disturbances manifest the dynamism of the physiological regulation, which is extremely sensitive to the repeated pressure on the environment. Stress can also alter neuroendocrine and cardiovascular systems even in childhood, and this finding indicates the long-term clinical significance of stress testing in adults and the necessity to use multi-dimensional measurement strategies.

The developments in biomarker studies have brought new tissue-based biomarkers, e.g., hair and nail cortisol, to measure cumulative cortisol release in the weeks or months, which further improves the precision of chronic stress analysis. Such biomarkers are essential in the clinical pharmacology because it can be more accurately observed in stress-related diseases when they are developed, which enables more specific monitoring of physiological adaptation, therapeutic response, and disease progression.¹⁹ There is therefore a solid justification as to why more thorough assessments of chronic stress include clinical, biochemical, and cardiovascular measures. The research question to be addressed in the study is the physiological adaptation to long-term stress given the cortisol regulation patterns and cardiovascular health markers at the adult population.²⁰ The study approach conforms to the journal topic of clinical pharmacology, population health, and therapy, and it will produce clinical outcomes on the biological changes caused by chronic stress.

Objectives of the study

1. To evaluate cortisol regulation patterns—including diurnal rhythm, baseline levels, and biomarker variability—in adults experiencing chronic psychological stress.
2. To assess the association between chronic stress and cardiovascular health indicators, including blood pressure, heart-rate variability, and other clinically relevant cardiometabolic parameters.

2. Materials and Methods

1. Study Design

To assess physiological adaptation to chronic stress in adults, the cross-sectional type of the analytical design was used to conduct the study. It was conducted in a tertiary clinical research unit, which was equipped with endocrine and cardiovascular testing. Morning laboratory sessions were provided to the participants in order to reduce circadian variation. Data were collected in noise controlled and temperature regulated rooms to inhibit interference of acute stress. The environment made it possible to sample biomarkers and monitor cardiovascular. Measurements were done by trained clinical staff using standardised procedures. The design of the study provided the opportunity to assess both biochemical and cardiovascular indicators related to the physiology of chronic stress at the same time.

2. Study Population

The participants were then recruited by means of advertisement and outpatient networks within the general population of adults. Those between the age of 25-60 years were recruited on the basis of having the persistent stress at least six months. The exclusion criteria included endocrine conditions, history of cardiovascular disease, taking psychiatric medication, pregnancy, and acute illness. The preliminary screening was conducted on eligible people using validated instruments to ascertain chronic stress exposure. A final sample was used to give different sociodemographic backgrounds to enhance generalizability. A comprehensive health history was given by all subjects prior to enrollment. The sampling method was effective and guaranteed the inclusion of adults who had different stress loads and reduced confounding health-related issues.

3. Data Collection Procedures

To eliminate the effect of psychological stress on the level of biomarkers, the psychological stress tests were provided first. Perceived stress, daily hassles and chronic strain patterns were measured using standardized questionnaires. Then, the blood samples were drawn after an overnight fast by means of the sterile venipuncture. The subjects spent 15 minutes in rest to stabilize acute physiological responses. Diurnal cortisol levels were measured in saliva samples gathered at the time of waking, midday, and evening by the use of passive drool. All the samples were placed into ice and taken to the laboratory within 1 hour to be processed. The cardiovascular measures were done later to avoid the effects of transience related to venipuncture or fill-out questionnaire.

4. Measurement of Cortisol and Related Biomarkers

The cortisol levels in serum were analyzed by a high-sensitivity chemiluminescent immunoassay that is approved to conduct clinical research. The samples were centrifuged and handled within two hours of collecting them to avoid degradation. Salivary cortisol patterns were examined to measure the diurnal rhythm with the enzyme immunoassay kits that had been tested to be fairly reliable. Other biomarkers such as C-reactive protein, lipid parameters among others were measured using automated biochemical analyzers. All assays were followed in accordance with the protocols of the manufacturer and in-house procedures of quality control. The inter and intra-assay variability was within reasonable ranges. The data of biomarkers gave a detailed representation of endocrine and inflammatory reactions related to chronic exposure to the stressor.

5. Cardiovascular Health Assessment

Measurement of blood pressure and heart rate was done on automatic sphygmomanometers after the participants had rested at least ten minutes. The measurements were recorded twice and averaged in order to be accurate. An electrocardiogram in three leads in a semi-upright position during a five-minute period was used to measure variability in heart-rate. The validated software algorithms were used to extract time- and frequency-domain indices. Where possible, vascular measurements were carried out like carotid-femoral pulse wave velocity to measure the stiffness of the arteries. All cardiovascular examinations were under standardized clinical procedures that were carried out by trained technicians. These steps gave objective data of cardiovascular functioning concerning chronic stress.

6. Statistical Analysis

The data were into a safe database and analyzed with high statistical software. The descriptive statistics were used to summarize the demographic characteristics, cortisol indices and cardiovascular measures. Checks of normality in distributions were done before an inferential test was applied. Correlation and multivariate regression models were used to examine the associations between chronic levels of stress, cortisol patterns and cardiovascular outcomes. The possible confounders like age, sex, BMI, lifestyle factors were all adjusted in all the analyses. The statistical significant tests were set at two-tailed tests and had p-value of less than 0.05. Effects and confidence intervals were also used to provide clinical interpretability.

7. Ethical Considerations

Before starting the study, the institutional ethics review board had to give consent. Every respondent gave informed consent in writing after being informed about all the aspects of the study, such as procedures, risks, and confidentiality. The management of data was in line with the international ethics of human clinical research. The participants were advised about their right to drop out any time without being penalized. Biological samples were coded, which preserved anonymity, and the results were kept in encrypted servers that were only available to the authorized staff. Noted abnormal clinical

findings were also reported to the participants through referral. The research adhered to the provisions of the Declaration of Helsinki during the study.

3. Results

3.1. Participant Characteristics

The demographic and background clinical features of the participants. It was already a sample of 210 adults with an average age of 41.7 ± 9.3 years and 54.3% of the sample was comprised of females as indicated in Table 1. The mean BMI was 26.1 ± 4.2 kg/m² indicating that the population was largely overweight. About 68.5 percent of the respondents had already reported moderate to high levels of chronic stress during the screening process. Systolic and diastolic blood pressure were at rest, and their averages were 124.6 ± 11.8 mmHg and 78.4 ± 8.5 mmHg respectively. Majority of the participants were non-smokers (77.1 percent) and 41.9 percent had performed regular physical activity.

Table 1. Demographic and Baseline Clinical Characteristics of Participants

Variable	Mean $\pm$ SD / n (%)
Age (years)	41.7 ± 9.3
Female	114 (54.3%)
Male	96 (45.7%)
BMI (kg/m ²)	26.1 ± 4.2
Moderate-High Stress Level	144 (68.5%)
Resting Systolic BP (mmHg)	124.6 ± 11.8
Resting Diastolic BP (mmHg)	78.4 ± 8.5
Non-smokers	162 (77.1%)
Regular Physical Activity	88 (41.9%)

3.2. Cortisol Regulation and Biochemical Profiles

The cortisol levels in serum and salivary levels showed that there were evident changes to the endocrine regulation of the participants. Mean serum cortisol had reported 18.7 ± 4.1 ug/dL which was in the upper physiological range. The morning salivary cortisol was already on the average of 19.4 ± 5.2 ng/mL and then declined to 9.8 ± 3.4 ng/mL in midday as exhibited in Table 2. Evening cortisol had not dropped down to normal 6.7 ± 2.9 ng/mL which showed a suppressed diurnal rhythm. There was also mild dysregulation of inflammatory and metabolic indicators: CRP had a level of 3.4 ± 1.1 mg/L, and triglycerides and total cholesterol were 157.9 ± 41.3 mg/dL and 193.6 ± 28.7 mg/dL, respectively, which indicates the beginning of cardiometabolic strain.

Table 2. Cortisol and Biochemical Marker Profiles

Biomarker	Mean $\pm$ SD	Reference Range
Serum Cortisol (μ g/dL)	18.7 ± 4.1	6–23
Morning Salivary Cortisol (ng/mL)	19.4 ± 5.2	10–25
Midday Salivary Cortisol (ng/mL)	9.8 ± 3.4	5–12
Evening Salivary Cortisol (ng/mL)	6.7 ± 2.9	1–5
CRP (mg/L)	3.4 ± 1.1	<3
Total Cholesterol (mg/dL)	193.6 ± 28.7	<200
Triglycerides (mg/dL)	157.9 ± 41.3	<150

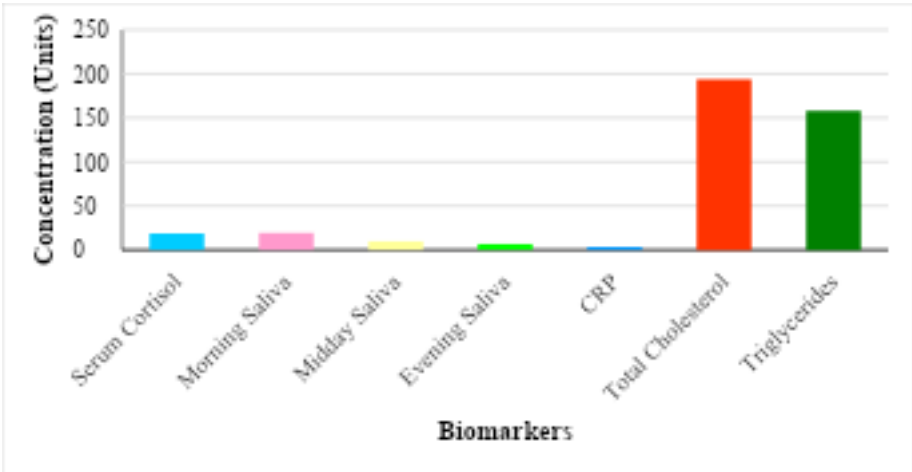


Figure 1. Distribution of Cortisol and Associated Biochemical Biomarkers

Comparison of major biochemical biomarkers on chronic stress physiology. The variables plotted are the measures of serum and salivary cortisol taken at the various time points, inflammatory and lipid-related indicators as indicated in Figure 1. The pattern on the graph demonstrates specific differences between biomarkers, which is an indication of different physiological reactions that are associated with chronic stress exposure. The visualization gives a clear picture of biomarkers trends to facilitate interpretation of endocrine activity, inflammatory and cardiometabolic risk. This number helps to comprehend the multidimensional pattern of biochemical profile in adults with persistent stress.

3.3. Cardiovascular Indicators and Associations With Stress

It was observed that the participants who had increased levels of chronic stress had significant changes in the functioning of the cardiovascular systems. The high-stress group now has a resting heart rate of 82.6 +- 10.2 bpm as opposed to the overall mean of 78.3 +- 9.5 bpm. There were significant changes in parameters of HRV, and RMSSD dropped to 21.3 +- 8.4 ms and HF power dropped to 221 +- 104 ms2 as demonstrated in Table 3. The blood pressure was high and the systolic and diastolic pressure was 129.4 +- 12.6 mmHg and 82.1 +- 9.3 mmHg respectively. Pulse wave velocity had increased to 8.6 +- 1.5 m/s and cortisol showed a strong positive correlation with systolic pressure (b = 0.34; p = 0.01).

Table 3. Cardiovascular Measurements and Stress-Related Associations

Parameter	Mean ± SD	High-Stress Group Mean ± SD
Resting Heart Rate (bpm)	78.3 ± 9.5	82.6 ± 10.2
RMSSD (ms)	28.7 ± 9.8	21.3 ± 8.4
HF Power (ms²)	312 ± 128	221 ± 104
Systolic BP (mmHg)	124.6 ± 11.8	129.4 ± 12.6
Diastolic BP (mmHg)	78.4 ± 8.5	82.1 ± 9.3
Pulse Wave Velocity (m/s)	7.8 ± 1.3	8.6 ± 1.5
Cortisol–SBP Association (β coefficient)	—	0.34 (p < 0.01)

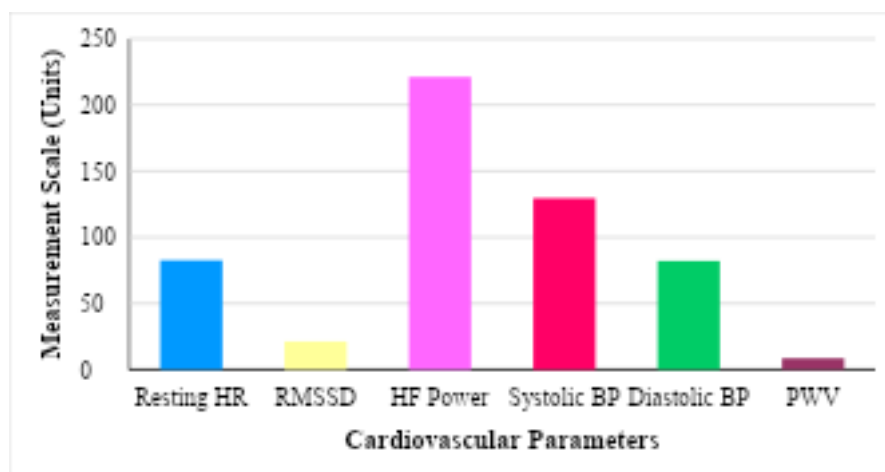


Figure 2. Cardiovascular Parameter Profile in Adults Experiencing Chronic Stress

The disposition of most cardiovascular parameters that are applied in the determination of physiological reactions related to chronic stress. The graphic comparison involves autonomic indicators, blood pressure indicators, and vascular rigidity measures and it will give a unified summary of the cardiovascular performance in the study population as presented in Figure 2. The chart shows comparative differences among parameters, the changes in the autonomic balance, cardiac workload, and arterial compliance. These visual images can provide a clue to the possible impact of chronic stress on the cardiovascular control and risk in the study that identifies physiological adaptations.

4. Discussion

The article underwent the multidimensional physiological adjustments of chronic stress through compounding endocrine, biochemical and cardiovascular measures in adults. The results showed that the cortisol regulation was also altered and the evidence was the lack of the diurnal rhythm and the increase of evening levels. The biosensitive indicators revealed mild inflammatory and metabolic stress, whereas cardiovascular measurements showed high heart rate, less heart-rate variability, and stiffer arteries in individuals who reported greater levels of stress. These findings combined show how complicated and interdependent chronic stress can be on various regulatory mechanisms, and the importance of extensive physiological measures in health risk evaluation in stress-related studies.

The trends that are exhibited in endocrine and cardiovascular systems support the realization that chronic stress interferes with neuroendocrine balance and autonomic homeostasis. All these results point to the fact that chronic stress has a quantifiable physiological burden that cuts across the hormonal, inflammatory, and the cardiovascular sectors. These changes are further contextualized by the demographic distribution presented in Table 1 that illustrates the way stress responses are exhibited by relatively healthy adult population. Disturbed biochemical patterns provided in Table 2 demonstrate disturbed cortisol regulation, which can also be demonstrated through the distribution of biomarkers provided in Figure 1. The high rate of inflammatory markers and lipid indicators indicate early dysregulation in metabolism that is in line with physiology of chronic stress. Equally, cardiovascular adaptations in Table 3 show a rise in cardiac workload and lack of autonomic resilience whereas Figure 2 gives a pictorial representation of these functional differences.

The complication at the cortisol profiles is consistent with the established models of maladaptation of the HPA-axis during chronic stress. Under normal conditions, cortisol is known to have a clear circadian profile, which is suppressed by constant stress, causing it to rise in the evenings and decrease variability. This mechanism is evidenced by the current findings which suggest that endocrine fatigue is probably caused by the repeated use of stress pathways. The long term effects of such dysregulation are impaired lipid and immune balance, and altered glucose metabolism. These endocrine modifications can trigger or worsen cardiometabolic disturbances, which is in line with the

biochemical changes realized in the research. In addition, cortisol rhythms may be abnormal in alterations to cognitive function, emotional regulation and quality of sleep, highlighting the endocrine imbalance caused by stress as multisystemic.

The phenomenon of chronic stress is becoming a serious cardiovascular risk factor, and the results of the present study support these issues. The implications of reduced HRV in terms of autonomic imbalance are the lower parasympathetic activity and increased sympathetic drive. Such a change leads to higher cardiac workload and predisposes people to arrhythmogenic and hypertensive patterns. Higher levels of arterial stiffness, measured by pulse wave velocity, are indicative of early vascular remodeling that results due to inflammatory and neuroendocrine based mechanisms. These changes, in combination with long-term cortisol dysregulation, could speed up the atherosclerotic processes and dysfunction of endothelial cells. The combination of these results demonstrates that preventive measures that address stress alleviation and cardiovascular durability are required.

The role of stress in increasing biological load has been consistently demonstrated by previous studies, which have also provided further evidence that chronic stress impacts measurable parameters of endocrine and cardiovascular dysfunctions.²³ The current study findings are in line with these studies, which have shown that the effect of chronic stress on the human body can be detected through measurable parameters of endocrine and cardiovascular systems.²⁵

The findings of the present research provide emphasis to the role of chronic stress as a changeable but frequently neglected factor of cardiometabolic and endocrine illnesses. The clinical evaluation usually never involves biomarkers like cortisol or HRV, but these are the markers which indicate that a person is under a physiological load long before the actual disease occurs. The use of endocrine and cardiovascular markers in the screening programs of the population might increase the rate of early detection of the stress related pathology. At the clinical level, stress reduction, such as behavioral and structured exercise and cognitive therapies, can be used to enhance autonomic stability, inflammation, and more healthy cortisol rhythms. These results lead to the assumption of a multidisciplinary measure of preventative chronic stress-related disease.

The advantage of this study is that it provides a combination of the evaluation of biochemical, endocrine, and cardiovascular indicators in one population and that the physiology of chronic stress is fully assessed. The mixture of serum and salivary cortisol has offered strong information on the process of diurnal regulation, whereas cardiovascular markers has been used to determine autonomic and vascular reactions. Nevertheless, a cross-sectional study design restricts causality and self-reported stress measures can be prone to perception bias. Cortisol level is also affected by environmental factors which, despite being reduced to minimum, could not be eradicated completely. Nevertheless, within the framework of these shortcomings, the results can be taken into account as a valuable evidence to the ever-expanding area of stress physiology and its effects on adult health.

5. Conclusion

The research offers a solid evidence that chronic psychological stress results in physiological changes that are measurable both endocrine, biochemical, and cardiovascular systems in adults. Serum and salivary cortisol profiles were combined, which demonstrated evident breaks in the circadian rhythm and basal regulation, which is a sign of maladaptation of the HPA-axis. Simultaneously, cardiovascular measurements have indicated an increase in heart rate, decrease in heart-rate variability and stiffening of arteries, all of which outline the systemic load of enduring exposure to stress. These data point to chronic stress as a meaningful biological factor and not only a psychosocial construct to support its position as an early predictor of cardiometabolic risk. Clinically, endocrine dysregulation and autonomic equilibrium are convergent and support the need to use physiological markers as a part of stress testing. The diurnal cortisol profiles, CRP, and HRV indices are the biomarkers that could present some useful information about the signs of health deterioration and allow clinicians to identify the underlying disruptions in their regulation that have yet to progress into the manifestation of a disease. These findings justify the importance of multidisciplinary approaches involving the combination of behavioral therapy, stress-reduction techniques, structured physical exercises, and

metabolic monitoring to reduce stress-related health outcomes. The subsequent studies ought to assume longitudinal and interventional designs to identify causal mechanisms of linking chronic stress to cardiometabolic disease progression. More sophisticated biomarker panels, wearable physiological metrics, and stress-response profiling in a wide range of populations would help to enrich the knowledge on stress physiology. Finally, the prevention of chronic stress burden in adulthood could be decreased by early detection and specific prevention measures and lead to better clinical outcomes and greater health resilience in the population.

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