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Article

Physical Activity, Metabolic Risk and the Primary Allostatic Load Mediators: An Explorative Study

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Abstract

Background: Chronic stress is associated with dysregulation of the body's allostatic systems, contributing to increased allostatic load (AL) and adverse metabolic outcomes. Regular physical activity (PA) is considered a key protective factor that may attenuate AL by enhancing adaptive stress responses and supporting metabolic health. This study examined the differences between PA, primary mediators of AL, and metabolic risk markers in apparently healthy adults in Germany. **Methods:** Forty-six adults (18 - 45 years) were categorized into moderate intensity (regular PA: ≥ 150 min a week vs non-regular PA: ≤ 150 min a week) group according to current PA recommendations. Primary AL mediators were quantified by cortisol ($\mu\text{g}/12\text{h}$), epinephrine ($\mu\text{g}/12\text{h}$), norepinephrine ($\mu\text{g}/12\text{h}$), and dehydroepiandrosterone sulfate (DHEA-S: $\mu\text{g}/\text{ml}$). Group differences in primary AL mediators and metabolic risk markers were examined using the Mann–Whitney U test. **Results:** A significant group difference was observed for cortisol levels, with higher values in the regular PA group ($p = 0.01$) with a moderate negative effect size of $r = -0.38$. No statistically significant differences ($p > 0.05$) were found between groups for epinephrine, norepinephrine, DHEA-S, or metabolic risk markers, including triglycerides, blood pressure, body mass index (BMI), and high-density lipoprotein cholesterol (HDL-C). **Conclusion:** The findings suggest that regular PA may be associated with altered stress-regulatory activity, as reflected by differences in cortisol. While no statistically significant group differences were observed for metabolic risk markers, descriptive patterns indicate more favorable lipid profiles and potential variation in primary AL mediators at higher PA levels. Given the exploratory nature of the analyses and the small and unequal group sizes, these findings should be interpreted with caution and warrant confirmation in future studies with larger and more balanced samples.

Keywords: allostatic load; exercise training; metabolic syndrome; primary mediators; stress

1. Introduction

Stress affects millions of people worldwide. The increasing prevalence of stress may be attributed to multiple factors, including environmental stressors, socioeconomic pressures, and unhealthy lifestyle changes [1,2]. Acute stress activates the sympathetic nervous system (SNS), leading to the release of epinephrine and norepinephrine and initiating the fight-or-flight response [3,4]. In contrast, chronic or prolonged stress predominantly activates the hypothalamic-pituitary-adrenal (HPA) axis [5,6]. This process involves hypothalamic release of corticotropin-releasing hormone (CRH), which stimulates adrenocorticotrophic hormone (ACTH) secretion from the pituitary and subsequently promotes cortisol release from the adrenal glands [7,8,9].

While acute stress responses are essential for physiological functioning and adaptation, chronic stress disrupts the body's regulatory systems and contributes to cumulative physiological strain [10].

This adaptive process, termed “allostasis”, describes how the body maintains stability through change [11,12]. However, prolonged or repeated exposure to stress results in cumulative “wear and tear” on physiological systems, a concept known as allostatic load (AL) [11,13,14]. Additionally, AL can be assessed using biomarkers across multiple physiological systems, with primary mediators reflecting immediate neuroendocrine responses to stress. These primary mediators include cortisol, epinephrine, norepinephrine, and dehydroepiandrosterone sulfate (DHEA-S) [15,16,17,18,19,20]. Chronic stress and elevated AL have been associated with the development of stress-related disorders and metabolic diseases, including metabolic syndrome (MetS) [1,21,22].

MetS is characterized by a cluster of cardiometabolic abnormalities, including elevated blood pressure, abdominal obesity, reduced high-density lipoprotein (HDL) cholesterol, increased triglycerides, and hyperglycemia [22,23]. Cortisol plays a central role in regulating glucose metabolism, immune function, and blood pressure. However, chronic elevations are associated with visceral adiposity, insulin resistance, and hypertension [24,25]. Similarly, sustained SNS activation, reflected by elevated epinephrine and norepinephrine levels, increases cardiometabolic risk through heightened heart rate, blood pressure, and vascular resistance [26,27]. DHEA-S acts as a counter-regulatory hormone that buffers the effects of cortisol, yet its levels often decline under chronic stress, further contributing to metabolic dysregulation [28,29].

Exercise is a subset of planned and repetitive physical activity (PA) performed to improve physical fitness and maintain health [30]. PA can be categorized into two types: exercise, which refers to engaging in high-intensity PA akin to that of an athlete (e.g., a minimum of 10 hours per week of training), and leisure sports, which involves moderate PA during recreational or leisure time [31]. Acute exercise acts as a stressor that temporarily activates the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system (SNS), resulting in transient increases in cortisol and catecholamines [32,24]. In contrast, regular endurance exercise and high-intensity interval training (HIIT) promote long-term adaptation, reducing resting levels of stress hormones and enhancing the efficiency of stress-responsive systems, possibly through enhanced catechol-O-methyltransferase (COMT) activity [24,33]. Collectively, regular PA supports improved stress recovery and physiological resilience by reducing HPA axis hyperactivity and lowering excessive SNS activation [34,35]. These adaptive mechanisms include better autonomic balance, increased endorphin release, and enhanced neuroplasticity [36], helping modulate AL and maintain metabolic regulation [37,38].

To better understand the pathophysiological mechanisms linking PA, AL, and metabolic risk, research in populations without diagnosed stress-related or metabolic diseases is warranted. The majority of AL research to date has focused on diseased populations, including individuals with depression or elevated AL, who often present with subclinical metabolic abnormalities such as impaired glucose tolerance or borderline hypertension that may progress to MetS [22,39,40,41,42]. In Germany, prior studies have demonstrated associations between MetS and stress-related conditions such as depression across age groups [40,41]. Exercise training has been shown to reduce MetS severity, depressive symptoms, and key metabolic risk markers, including body mass index (BMI), systolic blood pressure, and waist circumference [43].

Despite evidence linking PA, AL, and metabolic risk, limited research in German populations has examined these associations in apparently healthy adults. This study addresses this gap by examining differences between PA, primary AL mediators, and metabolic risk markers in an apparently healthy German adult population.

2. Materials and Methods

2.1. Study Design

The analysis is based on data from parallel study 3 (i.e., PSA 3 study) within the National Research Network, “Medicine in Spine Exercise (MiSpEx) Network” [44,45]. The PSA 3 was a study on psychometric and biological measures in adults. The PSA 3 was a longitudinal observational study with measurement time points (M1–M4) taken every four months between August 2013 and June

2015 [45,46]. The PSA 3 study data were collected using standardized questionnaires (M1–M4) and biomarkers from hair, blood, and urine (M1, M4), with laboratory assessments conducted by trained nurses. For collection procedures for urine and blood samples, check [45,46]. For the current study, a subsample ($n = 46$) of the baseline data (M1) was used. Additionally, the parent longitudinal design improved data quality and internal validity by ensuring that all measurements were gathered using consistent, protocol-driven techniques [45]. The baseline analysis offers a methodologically sound snapshot of early physiological dysregulation. This is in line with the study's aim of characterizing preclinical associations in people without any identified metabolic disorder, even though longitudinal analyses were outside the purview of this current investigation.

2.2. Study Population

Participants were recruited from the Ernst von Bergmann clinic and the University of Potsdam outpatient clinic, with a final sample of $n = 140$ individuals aged 18 to 45 years included in the study. As an incentive, participants received their clinical laboratory findings and a personalized stress profile upon study completion [45]. The participants included in this current study were able to complete a German questionnaire and did have at least one episode of non-specific low back pain (LBP) lasting four or more days within the previous 12 months. As no diagnosed cardiovascular or metabolic diseases were present [45], participants were classified as “apparently healthy” within the context of the present study. Exclusion criteria were pregnancy, acute infections, hormone therapy, or the use of specific medications (such as glucocorticoids and antibiotics); certain diseases (such as cardiovascular, metabolic, thyroid, vascular, malignant, lung, or autoimmune diseases); hemophilia; and psychological disorders (such as those listed in ICD-10: F70–79) and hair shorter than 2 cm [45]. For the present analysis, a subsample of $n = 46$ who had completed the AL biomarker assessment was used [45].

2.3. Ethical Approval

The study was carried out in compliance with the values outlined in the Declaration of Helsinki of 1975, as revised in 2013. A study nurse provided written and spoken information about the study to each participant before they all signed the written informed consent form. The main institutional ethics review board of the University of Potsdam, Germany, granted the final ethical approval on May 6, 2013 (No. 44/2012).

2.4. Physical Activity Assessments

A self-structured PA questionnaire was designed to capture weekly frequency and durations of PA domains, consistent with World Health Organization (WHO) PA guidelines [47]. High-intensity PA (labelled as exercise) was defined as above 10 hours a week, and leisure sport was defined as below 10 hours a week within the MiSpEx Network [44]. The instruments were tested for reliability and validity in several pilot studies conducted in the context of developing multiple randomized controlled trials before being implemented. The MiSpEx network randomised controlled trials were registered as DRKS00004977 [48] and DRKS00010129 [49] in the German Clinical Trials Register. Leisure sports was calculated as the product of time (min) and days spent performing activities such as walking, stair climbing, and cycling. Similarly, exercise was calculated as the product of time (min) and days spent performing exercise training (e.g., football, judo, swimming, basketball, etc.). Furthermore, an additional scale was calculated for the total PA (PA, min/wk), which was the product of days and time (min) spent performing both exercise and leisure sports. Based on total PA, study participants were categorized into two groups: regular PA ($n = 37$, ≥ 150 minutes/week) and non-regular PA ($n = 8$, ≤ 150 minutes/week) groups in accordance with WHO recommendations for health promotion. This categorical approach was done to reduce sensitivity to recall error and bias and thus align exposure classification with established public health thresholds [47].

2.5. Primary Mediators of Allostatic Load Assessment

12-h urinary cortisol ($\mu\text{g}/12\text{h}$) was assessed via enzyme-linked immunosorbent assay (ELISA, RE52241, ILB International GmbH, Germany). Serum DHEAS ($\mu\text{g}/\text{ml}$) was assessed via ELISA (RE52181, TECAN Hydro Flex, ILB International GmbH Germany) [45]. 12-h overnight urinary epinephrine ($\mu\text{g}/12\text{h}$) and norepinephrine ($\mu\text{g}/12\text{h}$) levels were assessed via ELISA (epinephrine RE59251, norepinephrine RE5926, both by ILB International GmbH Germany) [45]. Cortisol, epinephrine, norepinephrine, and DHEA-S were computed to calculate the primary allostatic load index (ALI). The primary (ALI) was constructed using a sample-based quartile, consistent with established methodology [45]. The AL biomarker values in the fourth quartile ($> 75\%$) of the parent cohort distribution were given a value of “1” (indicating relatively higher physiological burden), while values below this threshold were given a value of “0” (unburdened) [45].

2.6. Blood Pressure Measurement

Outpatient nurses measured systolic and diastolic blood pressure at three different times, with a 30-second rest interval in between each measurement. The readings of the second and third were averaged to provide the final blood pressure readings. The measurement was taken with a BOSO BS 90 Blood pressure device (BOSCH + SOHN GmbH u. Co., KG, Jungingen, Germany) [45, 46].

2.7. Lipid and Glucose Metabolic Biomarkers

Using enzymatic colorimetric assays (ABBOTT Architect ci8200; Abbott Laboratories, IL, USA), triglycerides, HDL-C, and LDL-C were measured. In addition, measurements of height (Seca 222 telescopic measuring rod; Seca AG, Switzerland), weight (Kern MPS scale; Kern & Sohn GmbH, Balingen, Germany), and waist/hip circumference (customary measuring tape) were taken [46]. The waist circumference was measured above the umbilicus at the narrowest point between the ribs and the iliac crest, and the hip circumference was measured at the widest point across the buttocks. The ratio of weight (kg) to height (m^2) was calculated for body mass index (BMI) [45, 46]. Glycosylated hemoglobin (HbA1c) was measured using high-performance liquid chromatography (HPLC) Bio-Rad Variant II (Bio-Rad Laboratories, CA, United States); fasting insulin was measured using an electrochemiluminescence enzyme immunoassay (ECLIA) using a Roche Cobas 8000 Modul E620 (Roche Diagnostics Ltd., Basel, Switzerland); and fasting glucose was measured by a hexokinase enzymatic reaction using a Roche Cobas 400 Plus (Roche Diagnostics Ltd., Basel, Switzerland) [45]. The following formula was used to compute insulin resistance [using the Homeostasis Model Assessment Index (HOMA)]: $\text{glucose [mg/dl]} \times \text{insulin [mU/ml]} / 405$ [45].

2.8. Statistical Analysis

Data was analyzed using the Statistical Package for Social Science (SPSS 29.0, Chicago, IL, USA) computer software. All primary mediators and metabolic risk markers were analyzed as continuous variables in group comparisons.

Normality was assessed using the Shapiro–Wilk test. As the distribution was skewed, a non-parametric statistical method was employed, as it is less sensitive to distributional assumptions and unequal group sizes. Descriptive data are presented in Table 1. Group comparisons between PA categories regarding primary mediators of AL and metabolic risk markers were conducted using the Mann–Whitney U test. The Mann–Whitney U test preserves rank-order information and does not require dichotomization of continuous data. This test was selected for its robustness for small and unequal sample sizes. Also, given the small and unequal sample size constraints, adjustment for multiple comparisons was not conducted. The analysis was rather considered exploratory and focused on effect direction and magnitude rather than inferential generalization. Adjustments for covariates such as sex, age, and BMI were not performed due to the small sample and unequal group sizes. This would have substantially increased the risk of model overfitting and unstable estimates.

Additionally, all missing datasets were excluded from the final analysis. The statistical significance level was set at $p < 0.05$.

3. Results

Finally, a total of $n = 46$ participants were included in the study (65.2% female, 32.6% male; median age = 30 years). Among them, 37 participants (80.4%) engaged in regular PA, and 97.4% additionally participated in leisure sports activities. One participant reported being physically active only through leisure sports. Regarding the biomarkers, all participants were within recommended normal or physiological ranges, such as for cortisol (mg/12h), epinephrine (mg/12h), norepinephrine (mg/12h), and DHEA-S (mg/ml). Applying metabolic risk markers, $n = 9$ (19.6%) of the sample were identified with elevated waist circumferences, $n = 4$ (8.7%) with elevated blood pressure, $n = 2$ (4.3%) with elevated blood glucose, $n = 2$ (4.3%) with elevated triglycerides, and an additional $n = 2$ (4.3%) with reduced HDL-C.

Group comparisons indicated differences between individuals who engage in regular PA and those who incorporate PA only occasionally into their daily routines (non-regular PA). Regularly active individuals exhibit approximately a fourfold higher level of activity (regular PA: $Mdn = 420$ min vs. non-regular PA: $Mdn = 135$ min; $U = 35.500$, $Z = -2.648$, $p = 0.008$). The higher physiological strain in this group is reflected in the primary AL mediator cortisol (regular PA: $Mdn = 130.60$ mg/12h vs. non-regular PA: $Mdn = 71.50$ mg/12h; $U = 61.00$, $Z = -2.583$, $p = 0.01$) with a moderate negative effect size of $r = -0.38$ (effect size calculation not included in Table 2). While cortisol differed between the groups, no corresponding significant differences ($p > 0.05$) were observed in metabolic risk markers such as triglycerides, blood pressure, waist circumference, fasting blood glucose, BMI, WC, and HDL-C between the two groups (see Table 2). No significant differences were observed between epinephrine, norepinephrine, and DHEA-S.

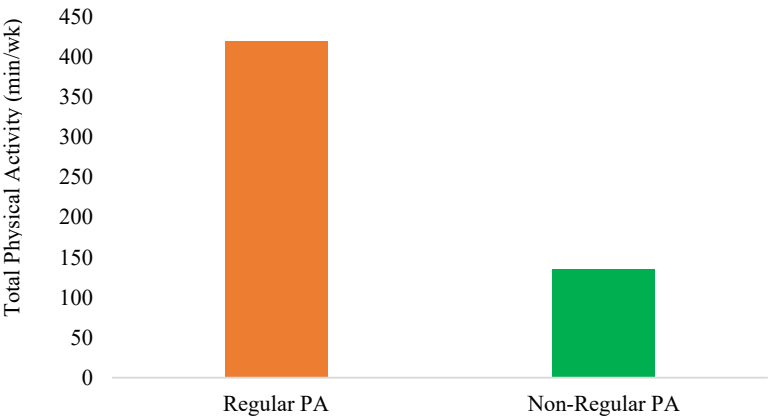


Figure 1. Differences in Total physical activity (min/wk) between regular PA and non-regular PA participants.

Table 1. Descriptive statistics of study participants (n = 46, 100%).

Variables	N	%	Median	IQR	Range
Age (years)	45	97.8	30.00	15.00	25.00
Sex					
Male	15	32.6	-	-	-
Female	30	65.2	-	-	-
Primary mediators of AL					
Cortisol (µg/12h)	46	100.0	113.55	73.70	238.60

Epinephrine (µg/12h)	46	100.0	5.95	5.30	16.80
Norepinephrine (µg/12h)	46	100.0	24.40	20.60	95.50
DHEA-S (µg/ml)	46	100.0	0.53	0.89	2.48
Primary ALI	46	100.0	1.00	2.00	4.00
Anthropometry					
BMI(kg/m²)	44	95.7	22.29	3.13	13.07
Waist circumference (cm)	45	97.8	75.20	13.00	42.30
Blood pressure					
Systolic blood pressure (mmHg)	45	97.8	100.00	13.75	50.00
Diastolic blood pressure (mmHg)	45	97.8	60.00	10.00	35.00
Lipid profile					
Triglycerides (mg/dl)	46	100.0	89.90	48.90	129.80
HDL-C (mg/dl)	46	100.0	62.25	17.60	59.50
Glycemia					
Fasting blood glucose (mg/dl)	46	100.0	86.30	7.40	29.40
Lifestyle habits					
Leisure Sports (min/week)	38	82.6	150.00	225.00	460.00
Exercise (min/week)	37	80.4	240.00	345.00	1275.00
Total Physical Activity (PA) (min/week)	43	93.5	330.00	453.00	1680.00

Key: DHEA-S: dehydroepiandrosterone sulfate; Primary ALI: primary allostatic load index; BMI: body mass index, WHR: waist-hip ratio; HDL-C: high density lipoprotein cholesterol; N: number; %: percentage; IQR: interquartile range. PA (leisure sports); PA (leisure sports). Exercise (high intense training more than 10 hours a week. Total Training Activity (sum of PA and exercise).

Table 2. Differences between Anthropometric and biomarkers between regular PA and non-regular PA group.

Variables	Regular PA				Non-regular PA				U	Z	p
	(n = 37)				(n = 8)						
	N (%)	Md n	Me an ran k	Su m of Me an ran ks	N (%)	Md n	M ea n ra nk	Sum of mea n rank s			
Age	37 (80.43)	28.00	22.07	816.50	8 (17.40)	37.50	27.31	218.50	110.500	-1.026	0.30
Sex											
Male	14	-	-	-	1	-	-	-	-	-	-

	(30.43)				(2.17)						
Female	23	-	-	-	7	-	-	-	-	-	-
	(50.00)				(15.22)						
Anthropometry											
BMI (kg/m²)	35	22.	22.6	792.	8	21.9	19.	154.0	118.0	-	0.4
	(76.08)	34	3	00	(17.40)	2	25	0	00	1.694	9
Waist circumference (cm)	36	75.	22.4	807.	8	79.1	22.	183.0	141.0	-	0.9
	(78.26)	60	2	00	(17.40)	0	88	0	00	.091	2
Primary Mediators of AL											
Cortisol (µg/12h)	37	130	25.3	938.	8	71.5	12.	97.00	61.00	-	0.0
	(80.43)	.60	5	00	(17.40)	0	13		0	2.583	1
Epinephrine (µg/12h)	37	7.0	24.2	898.	8	4.40	17.	137.0	101.0	-	0.1
	(80.43)	0	7	00	(17.40)		13	0	00	1.396	6
Norepinephrine (µg/12h)	37	25.	23.8	884.	8	19.0	18.	151.0	115.0	-	0.3
	(80.43)	30	9	00	(17.40)	0	88	0	00	.980	2
DHEA-S (µg/ml)	37	0.5	22.3	828.	8	0.69	25.	207.0	125.0	-	0.4
	(80.43)	0	8	00	(17.40)		88	0	00	.683	9
Primary ALI	37	1.0	23.4	866.	8	0.50	21.	169.0	133.0	-	0.6
	(80.43)	0	1	00	(17.40)		13	0	00	.473	3
Blood Pressure											
Systolic blood pressure (mmHg)	36	100	21.6	780.	8	102.	26.	209.5	114.5	-	0.3
	(78.26)	.00	8	50	(17.40)	50	19	0	00	.909	6
Diastolic blood pressure (mmHg)	36	60.	22.3	805.	8	60.0	23.	185.0	139.0	-	0.8
	(78.26)	00	6	00	(17.40)	0	13	0	00	.167	6

Lipid Profiles											
Triglycerides (mg/dl)	37 (80.43)	87.70	21.58	798.50	8 (17.40)	110.95	29.56	236.50	95.500	-1.559	0.11
HDL-C (mg/dl)	37 (80.43)	65.70	23.84	882.00	8 (17.40)	59.55	19.13	153.00	117.000	-.921	0.35
Glycemia											
Fasting blood Glucose (mg/dl)	37 (80.43)	86.30	22.61	836.50	8 (17.40)	86.05	24.81	198.50	133.500	-.431	0.66
Total Physical Activity (min/wk)	37 (80.43)	420.00	24.04	889.50	6 (13.04)	135.00	9.42	56.500	35.500	-2.648	0.08

Key: DHEA-S: dehydroepiandrosterone sulfate; Primary ALI: primary allostatic load index; PA (leisure sports); Exercise (high intense training more than 10 hours a week; Total Training Activity (sum of PA and exercise); Mdn: median; BMI, body mass index; WHR: waist-hip ratio; HDL-C: high density lipoprotein cholesterol. Significant at $p < 0.05$.

4. Discussion

The present study investigated the different PAs on the primary mediators of AL and metabolic risk markers in apparently healthy adults. Individuals who engaged in regular PA demonstrated an approximately fourfold higher activity level compared to the non-regularly PA group. In the regular PA group, the total PA (min/week) was ($Mdn = 420$ min/week). The current descriptive findings align with these data and underscore the preventive relevance of maintaining consistent PA across adulthood.

Additionally, the higher physiological strain in the regularly PA group is reflected in significantly elevated cortisol levels, as well as slight increases in epinephrine and norepinephrine levels. Although regular PA is often associated with improved stress regulation [24,33,37,38], elevated cortisol in this context may be a reflection of adaptive neuroendocrine engagement rather than pathological dysregulation [7]. Notably, the repeated stress from exercise training frequently activates the HPA axis, leading to ACTH hypersecretion due to adrenal enlargement, which triggers cortisol release. On one hand, this can result in higher basal and exercise-induced cortisol levels as the body becomes more efficient in responding to stress [24,50]. On the other hand, excessive and high-intensity exercise training without adequate recovery may lead to overtraining syndrome, which results from prolonged HPA axis activation and disrupted circadian rhythms [51,52]. In this current study, a more detailed analysis of the descriptive data reveals that presented cortisol levels may be influenced by the volume and intensity of exercising. This finding aligns with other studies, which have reported higher cortisol levels in individuals who engage in exercise training compared to those who do not participate in exercise training [24,51]. This phenomenon can be attributed to the exercise-induced glucocorticoid paradox, where elevated cortisol may reflect an adaptive neuroendocrine activation instead of pathology [53]. Interestingly, within the AL framework, higher cortisol does not necessarily indicate harm but may signal sustained HPA axis activation in response to repeated physiological demands [7]. In this sample, regular PA, particularly at higher volumes

(~420 min/week), may impose cumulative stress when recovery, sleep, or psychosocial context are not accounted for. This warrants cautious interpretation of the current findings.

In comparing the two groups (i.e., regular PA vs non-regular PA), no significant group differences were observed for epinephrine, norepinephrine, primary ALI, and DHEA-S. Interestingly, similar results have been found in other studies [54,55]. It should be noted that during both acute stress and exercise, epinephrine is released into the bloodstream from the adrenal medulla as a result of SNS activation [32]. This triggers the body for energy mobilization by stimulating lipolysis, hepatic glucose output, and suppression of insulin secretion through the β -adrenergic signaling pathways [34,56]. In physically active individuals, acute or moderate increases in epinephrine have been shown to be associated with enhanced metabolic flexibility and reduced central adiposity [57,58]. Additionally, regular PA improves norepinephrine activity and function resulting from an adaptive response to the HPA axis and catecholamines by the activity of COMT [24,33,59].

Epinephrine enhances fat oxidation and thermogenesis, resulting in lower visceral fat accumulation, which is one of the key components of MetS [60]. Long-term PA participation does not only temporarily increase epinephrine levels during exercise but also improves β -adrenergic sensitivity and mitochondrial efficiency in skeletal muscle. This contributes to better glucose absorption and insulin sensitivity [61]. As described in the stress physiology framework, catecholamines serve as primary mediators of allostatic responses [26,27]. Importantly, the observed catecholamine patterns in this current study are interpreted within the AL framework. Both urinary epinephrine and norepinephrine serve as indicators of neuroendocrine activity associated with physiological stress regulation [44,45]. The findings reflect neuroendocrine activity at the time of assessment that may be associated with regular PA participation. The findings are consistent with prior research suggesting that PA may be associated with altered catecholamine signaling linked to metabolic regulation, including reduced insulin antagonism and enhanced lipolytic processes [57,58]. However, these associations should be interpreted cautiously, as stress responses to PA vary depending on exercise intensity, duration, and modality [24,33,59], and causal relationships cannot be inferred due to the cross-sectional design of the current study.

Anthropometric measures such as BMI and waist circumference did not differ significantly between groups. However, the regular PA group showed numerically lower triglyceride levels and higher HDL-C concentrations compared with the non-regular PA group. This pattern is consistent with existing evidence linking PA to improved lipid metabolism, even in the absence of statistically significant differences in lipid and glycemic markers [62]. In line with studies demonstrating vascular and autonomic benefits of regular exercise, both groups exhibited similarly low systolic and diastolic blood pressure values [63]. Together, these findings support the notion that regular PA contributes to the maintenance of metabolic homeostasis through neuroendocrine and cardiovascular pathways.

Within the AL framework, this pattern may reflect early compensatory physiological responses rather than established metabolic dysregulation. From a theoretical perspective, prolonged stress exposure can lead to cumulative physiological dysregulation across immunological, metabolic, and neuroendocrine systems [12,13,14,64]. PA represents a key behavioral regulator of these processes. Exercise enhances systemic flexibility and reduces basal allostatic load by introducing acute, manageable stressors that recalibrate sympathetic nervous system activity and the HPA axis [37,38]. These adaptations may mitigate the development of MetS by improving insulin sensitivity, lipid turnover, and endothelial function [29,36,65,66,67].

Nevertheless, elevated blood glucose, waist circumference, triglycerides, and reduced HDL-C were observed in a subset of participants, indicating that subclinical cardiometabolic risk markers can be present even in apparently healthy individuals and may contribute to later development of MetS [42]. Accordingly, preventive strategies—including regular PA and routine medical check-ups—remain important even in healthy populations, particularly to identify and manage latent risk profiles such as genetically predisposed lipid metabolism abnormalities.

The current study has limitations that should be considered by future researchers. This was a secondary data analysis. Thus, the reliance on self-reported PA, the small sample size, gender imbalance favoring females, and cross-sectional sample limits causal inference, analysis methods, and generalization. Additionally, the absence of correction for multiple comparisons may increase the risk of type I error [68]. Accordingly, the results should be interpreted as exploratory and hypothesis-generating. Although relevant covariates such as age, sex, diet, sleep, BMI, and timing of cortisol sampling were available in the dataset, adjustment for these variables was not performed due to the small and unequal subsample size, which would have substantially increased the risk of model overfitting and unstable estimates. Therefore, causal interpretation of the observed associations is limited, and future studies with larger samples are warranted to confirm these findings [69,70,71]. Also, information concerning the number of years the participants have been participating in PA was unknown; hence, care should be taken when interpreting the results. Future research should replicate these findings with larger, longitudinal cohorts and multimethod PA assessments to enhance validity. Additionally, there are different scoring procedures and biomarkers used in calculating primary ALI [17,19]. This could lead to different outcomes. In the current study, ALI was calculated from [72]. However, assessing AL across the various neuroendocrine systems is complex and warrants further research.

5. Conclusions

In conclusion, findings from this exploratory investigation indicate that regular PA may be associated with altered stress-regulatory activity, as reflected by higher cortisol levels alongside stable secondary metabolic risk markers. Differences in triglycerides and HDL-C were observed numerically, but group differences in metabolic risk markers were not statistically significant. However, given the cross-sectional design, small sample size, and methodological limitations, these findings should be interpreted as exploratory and hypothesis-generating. Future longitudinal studies with larger samples and with adequate power are needed to clarify how sustained PA influences neuroendocrine function, allostatic processes, and long-term metabolic health.

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Data Availability Statement: Data containing potentially identified or sensitive patient information is restricted by European law (GDPR). The data used in this study containing clinical participants is unavailable in a public repository. However, data are available upon reasonable request to Pia-Maria Wippert (wippert@uni-potsdam.de).

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Abbreviations

The following abbreviations are used in this manuscript:

ACTH	Adrenocorticotrophic Hormone
AL	Allostatic load
ALI	Allostatic load Index
BMI	Body Mass Index
COMT	Catechol-O-Methyltransferase
CRH	Corticotropin-Releasing Hormone
DHEAS	Dehydroepiandrosterone sulfate
HDL-C	High Density Lipoprotein Cholesterol
HIIT	High Intensity Interval Training
HOMA	Homeostasis Model Assessment Index
HPA axis	Hypothalamic-Pituitary-Adrenal Axis
LBP	Low Back Pain
LC/NE	Locus Coeruleus/norepinephrine System
LDL-C	Low Density Lipoprotein Cholesterol
MiSpEx	Medicine in Spine Exercise Network
PA	Physical Activity
PSA 3	Parallel Study 3
SNS	Sympathetic Nervous System
VAS	Visual Analogue Scale
WHO	World Health Organization

References

1. Kivimäki, M.; Bartolomucci, A.; Kawachi, I. The multiple roles of life stress in metabolic disorders. *Nat. Rev. Endocrinol.* 2023, 19 (1), 10–27. <https://doi.org/10.1038/s41574-022-00746-8>

2. Kumar, R.; Rizvi, M. R.; Saraswat, S. Obesity and stress: a contingent paralysis. *Int. J. Prev. Med.* 2022, 13, 95. https://doi.org/10.4103/ijpvm.IJPVM_427_20

3. Won, E.; Kim, Y. K. Stress, the autonomic nervous system, and the immune-kynurenine pathway in the etiology of depression. *Curr. Neuroparmacol.* 2016, 14 (7), 665–673. <https://doi.org/10.2174/1570159x14666151208113006>

4. Ebert, S. N.; Rong, Q.; Boe, S.; Thompson, R. P.; Grinberg, A.; Pfeifer, K. Targeted insertion of the Cre-recombinase gene at the phenylethanolamine N-methyltransferase locus: a new model for studying the developmental distribution of adrenergic cells. *Dev. Dyn.* 2004, 231 (4), 849–858. <https://doi.org/10.1002/dvdy.20188>

5. Mbiydzanyuy, N. E.; Qulu, L. A. Stress, hypothalamic-pituitary-adrenal axis, hypothalamic-pituitary-gonadal axis, and aggression. *Metab. Brain Dis.* 2024, 39 (8), 1613–1636. <https://doi.org/10.1007/s11011-024-01393-w>

6. Ring, M. An integrative approach to HPA axis dysfunction: from recognition to recovery. *Am. J. Med.* 2025, 138 (10), 1451–1463. <https://doi.org/10.1016/j.amjmed.2025.05.044>

7. James, K. A.; Stromin, J. I.; Steenkamp, N.; Combrinck, M. I. Understanding the relationships between physiological and psychosocial stress, cortisol and cognition. *Front. Endocrinol.* 2023, 14, 1085950. <https://doi.org/10.3389/fendo.2023.1085950>

8. Molina-Hidalgo, C.; Stillman, C. M.; Collins, A. M.; Velazquez-Diaz, D.; Ripperger, H. S.; Drake, J. A.; Gianaros, P. J.; Marsland, A. L.; Erickson, K. I. Changes in stress pathways as a possible mechanism of aerobic exercise training on brain health: a scoping review of existing studies. *Front. Physiol.* 2023, 14, 1273981. <https://doi.org/10.3389/fphys.2023.1273981>

9. Kageyama, K.; Iwasaki, Y.; Daimon, M. Hypothalamic regulation of corticotropin-releasing factor under stress and resilience. *Int. J. Mol. Sci.* 2021, 22, 12242. <https://doi.org/10.3390/ijms22212242>

10. Malhotra, N.; Sinha, P.; Rathoria, R.; Rathoria, E. Corticotropin-releasing hormone. In *FOGSI Focus on Harmony of Hormones*; Evangel Publishing, 2024.

11. Word, K. R.; Austin, S. H.; Wingfield, J. C. Allostasis revisited: a perception, variation, and risk framework. *Front. Ecol. Evol.* 2022, *10*, 954708.

12. Sterling, P.; Eyer, J. Allostasis: a new paradigm to explain arousal pathology. In *Handbook of Life Stress, Cognition and Health*; Fisher, S., Reason, J., Eds.; Wiley: New York, **1988**; pp 629–649.

13. Juster, R. P.; McEwen, B. S.; Lupien, S. J. Allostatic load biomarkers of chronic stress. *Neurosci. Biobehav. Rev.* 2010, *35* (1), 2–16. <https://doi.org/10.1016/j.neubiorev.2009.10.002>

14. McEwen, B. S.; Stellar, E. Stress and the individual. Mechanisms leading to disease. *Arch. Intern. Med.* 1993, *153* (18), 2093–2101.

15. Bailey, A.; Payton, A.; Fleming, J.; Rager, J. E.; Jaspers, I. A novel approach for measuring allostatic load highlights differences in stress burdens due to race, sex and smoking status. *PLoS One* 2025, *20*, e0323788. <https://doi.org/10.1371/journal.pone.0323788>

16. Seeman, T. E.; McEwen, B. S.; Rowe, J. W.; Singer, B. H. Allostatic load as a marker of cumulative biological risk: MacArthur studies of successful aging risk. *Proc. Natl. Acad. Sci. U.S.A.* 2001, *98* (8), 4770–4775.

17. Beckie, T. M. A systematic review of allostatic load, health, and health disparities. *Biol. Res. Nurs.* 2012, *14* (4), 311–346. doi:10.1177/1099800412455688

18. Sun, J.; Wang, S.; Zhang, J. Q.; Li, W. Assessing the cumulative effects of stress: The association between job stress and allostatic load in a large sample of Chinese employees. *Work Stress* 2007, *21* (4), 333–347. doi: 10.1080/02678370701742748

19. Goldman, N.; Turra, C. M.; Gleib, D. A.; Lin, Y. H.; Weinstein, M. Physiological dysregulation and changes in health in an older population. *Exp. Gerontol.* 2006, *41* (9), 862–870. <https://doi.org/10.1016/j.exger.2006.06.050>

20. Seplaki, C. L.; Goldman, N.; Gleib, D.; Weinstein, M. A comparative analysis of measurement approaches for physiological dysregulation in an older population. *Exp. Gerontol.* 2005, *40* (5), 438–449. <https://doi.org/10.1016/j.exger.2005.03.002>

21. Chourpiliadis, C.; et al. Metabolic Profile and Long-Term Risk of Depression, Anxiety, and Stress-Related Disorders. *JAMA Netw. Open* 2024, *7*, e244525. <https://doi.org/10.1001/jamanetworkopen.2024.4525>

22. Osei, F.; Block, A.; Wippert, P. M. Association of primary allostatic load mediators and metabolic syndrome (MetS): A systematic review. *Front. Endocrinol.* 2022, *13*, 946740. <https://doi.org/10.3389/fendo.2022.946740>

23. Alberti, K. G.; et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* **2009**, *120*, 1640–1645. doi:10.1161/CIRCULATIONAHA.109.192644.

24. Athanasiou, N.; Bogdanis, G. C.; Mastorakos, G. Endocrine responses of the stress system to different types of exercise. *Rev. Endocr. Metab. Disord.* 2023, *24* (2), 251–266. <https://doi.org/10.1007/s11154-022-09758-1>

25. Zhao, X., An, X., Yang, C., Sun, W., Ji, H., Lian, F. The crucial role and mechanism of insulin resistance in metabolic disease. *Front. Endocrinol.* 2023, *14*, 1149239. <https://doi.org/10.3389/fendo.2023.1149239>

26. Lambert, G. W.; Patel, M.; Lambert, E. A. The Influence of the Sympathetic Nervous System on Cardiometabolic Health in Response to Weight Gain or Weight Loss. *Metabolites* 2025, *15*, 286. <https://doi.org/10.3390/metabo15050286>

27. Ziegler, K. A.; Engelhardt, S.; Carnevale, D.; McAlpine, C. S.; Guzik, T. J.; Dimmeler, S.; Swirski, F. K. Neural Mechanisms in Cardiovascular Health and Disease. *Circ. Res.* 2025, *136* (11), 1233–1261. <https://doi.org/10.1161/CIRCRESAHA.125.325580>

28. Erceg, N., Micic, M., Forouzan, E., Knezevic, N. N. (2025). The Role of Cortisol and Dehydroepiandrosterone in Obesity, Pain, and Aging. *Diseases* 2025, *13*, 42. <https://doi.org/10.3390/diseases13020042>

29. Heaney, J. L.; Carroll, D.; Phillips, A. C. DHEA and cortisol responses to acute stress in healthy humans. *J. Endocrinol.* 2012, *215* (3), 419–429. <https://doi.org/10.1530/JOE-12-0231>

30. Martínez-Vizcaino, V., Caverio-Redondo, I., Reina-Gutiérrez, S., Gracia-Marco, L., Gil-Cosano, J. J., Bizzozero-Peroni, B., Rodriguez-Artalejo, F., Ubago-Guisado, E. Comparative effects of different types of

- exercise on health-related quality of life during and after active cancer treatment: A systematic review and network meta-analysis. *J. Sport Health Sci.* 2023, 12 (6), 726–738. <https://doi.org/10.1016/j.jshs.2023.01.002>
31. Bull, F. C.; et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *Br. J. Sports Med.* 2020, 54 (24), 1451–1462. <https://doi.org/10.1136/bjsports-2020-102955>
 32. Çınar, V., Bağ, M. F., Aslan, M., Çınar, F., Gennaro, A., Akbulut, T., Migliaccio, G. M. Impact of different exercise modalities on neuroendocrine well-being markers among university students: a study of renalase and catecholamine responses. *Front. Physiol.* 2025, 16, 1591132. <https://doi.org/10.3389/fphys.2025.1591132>
 33. Bogdanis, G. C., Philippou, A., Stavrinou, P. S., Tenta, R., Maridaki, M. Acute and delayed hormonal and blood cell count responses to high-intensity exercise before and after short-term high-intensity interval training. *Res. Sports Med.* 2022, 30 (4), 400–414. <https://doi.org/10.1080/15438627.2021.1895783>
 34. Daniela, M., Catalina, L., Ilie, O., Paula, M., Daniel-Andrei, I., Ioana, B. Effects of Exercise Training on the Autonomic Nervous System with a Focus on Anti-Inflammatory and Antioxidants Effects. *Antioxidants* 2022, 11, 350. <https://doi.org/10.3390/antiox11020350>
 35. Heaney, J. L.; Carroll, D.; Phillips, A. C. DHEA, DHEA-S and Cortisol Responses to Acute Exercise in Older Adults in Relation to Exercise Training Status and Sex. *Age* 2013, 35 (2), 395–405. DOI: 10.1007/s11357-011-9345-y.
 36. Ribeiro, D., Petrigna, L., Pereira, F. C., Muscella, A., Bianco, A., Tavares, P. The Impact of Physical Exercise on the Circulating Levels of BDNF and NT 4/5: A Review. *Int. J. Mol. Sci.* 2021, 22, 8814. <https://doi.org/10.3390/ijms22168814>
 37. D'Alessio, L., Korman, G. P., Sarudiansky, M., Guelman, L. R., Scévola, L., Pastore, A., Obregón, A., Roldán, E. J. A. Reducing Allostatic Load in Depression and Anxiety Disorders: Physical Activity and Yoga Practice as Add-On Therapies. *Front. Psychiatry* 2020, 11, 501. <https://doi.org/10.3389/fpsy.2020.00501>
 38. McEwen B. S. (2007). Physiology and neurobiology of stress and adaptation: central role of the brain. *Physiol. Rev.* 2007, 87 (3), 873–904. <https://doi.org/10.1152/physrev.00041.2006>
 39. Osei, F., Wippert, P. M., Block, A. Allostatic Load and Metabolic Syndrome in Depressed Patients: A Cross-Sectional Analysis. *Depress. Anxiety* 2024, 1355340. <https://doi.org/10.1155/2024/1355340>
 40. Wiltink, J.; Beutel, M.E.; Tillmann, P.S.; Wild, P.S.; Münzel, T.; Lackner, K.J.; Pfeiffer, N.; Michal, M.; Schulz, A. Associations between degree and sub-dimensions of depression and metabolic syndrome (MetS) in the community: results from the Gutenberg Health Study (GHS). *BMC Psychiatry* 2018, 18, 114. <https://doi.org/10.1186/s12888-018-1691-1>
 41. Block, A., Schipf, S., Van der Auwera, S., Hannemann, A., Nauck, M., John, U., Grabe, H. J. Sex and age-specific associations between major depressive disorder and metabolic syndrome in two general population samples in Germany. *Nord. J. Psychiatry* 2016, 70 (8), 611–620. <https://doi.org/10.1080/08039488.2016.1191535>
 42. Gruenewald, T. L., Karlamangla, A. S., Hu, P., Stein-Merkin, S., Crandall, C., Koretz, B., Seeman, T. E. (2012). History of socioeconomic disadvantage and allostatic load in later life. *Soc. Sci. Med.* 2012, 74 (1), 75–83. <https://doi.org/10.1016/j.socscimed.2011.09.037>
 43. Haufe, S., et al. Telemonitoring-supported exercise training, metabolic syndrome severity, and workability in company employees: a randomised controlled trial. *Lancet Public Health.* 2019, 4 (7), e343–e352.
 44. Mayer F, Arampatzis A, Banzer W, Beck H, Brüggemann G-P, Hasenbring M, Kellmann M, Kleinert J, Schiltenswolf M, Schmidt H, Schneider C, Stengel D, Wippert P-M, Platen P. Medicine in Spine Exercise [MiSpEx] – a national research network to evaluate back pain. *Dtsch Z Sportmed.* 2018; 69: 229-235. doi:10.5960/dzsm.2018.340
 45. Wippert, P. M., Puerto Valencia, L., Drießlein, D. Stress and Pain. Predictive (Neuro)Pattern Identification for Chronic Back Pain: A Longitudinal Observational Study. *Front. Med.* 2022, 9, 828954. <https://doi.org/10.3389/fmed.2022.828954>
 46. Wippert, P.-M., Honold, J., Wang, V., & Kirschbaum, C. Assessment of chronic stress: Comparison of hair biomarkers and allostatic load indices. *Psychol. Res.* 2014, 4 (7), 517–524. <https://doi.org/10.17265/2159-5542/2014.07.001>
 47. Bull, F. C., et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *Br. J. Sports Med.* 2020, 54 (24), 1451–1462. <https://doi.org/10.1136/bjsports-2020-102955>

48. Wippert, P.-M.; Niederer, D.; Drießlein, D.; Beck, H.; Banzer, W.; Schneider, C.; Schiltenswolf, M.; Mayer, F. Psychosocial Moderators and Mediators of Sensorimotor Exercise in Low Back Pain: A Randomized Multicenter Controlled Trial. *Front. Psychiatry* **2021**, *12*, 629474.
49. Niederer, D.; Vogt, L.; Wippert, P.-M.; Puschmann, A. K.; Pfeifer, A. C.; Schiltenswolf, M.; Banzer, W.; Mayer, F. Medicine in spine exercise (MiSpEx) for nonspecific low back pain patients: study protocol for a multicentre, single-blind randomized controlled trial. *Trials* **2016**, *17*, 507
50. Zouhal, H., Jacob, C., Delamarche, P., Gratas-Delamarche, A. Catecholamines and the effects of exercise, training and gender. *Sports Med.* 2008, *38* (5), 401–423. <https://doi.org/10.2165/00007256-200838050-00004>
51. Kreher JB, Schwartz JB. Overtraining syndrome: a practical guide. *Sports Health* 2012, *4* (2), 128–138. doi:10.1177/1941738111434406
52. Fiala O, Hanzlova M, Borska L, Fiala Z, Holmannova D. Beyond physical exhaustion: Understanding overtraining syndrome through the lens of molecular mechanisms and clinical manifestation. *Sports Med. Health Sci.* 2025, *7* (4), 237–248. doi:10.1016/j.smhs.2025.01.006
53. Chen, C., Nakagawa, S., An, Y., Ito, K., Kitaichi, Y., Kusumi, I. The exercise-glucocorticoid paradox: How exercise is beneficial to cognition, mood, and the brain while increasing glucocorticoid levels. *Front. Neuroendocrinol.* 2017, *44*, 83–102. <https://doi.org/10.1016/j.yfrne.2016.12.001>
54. Hamer, M., Steptoe, A. Cortisol responses to mental stress and incident hypertension in healthy men and women. *J. Clin. Endocrinol. Metab.* 2012, *97* (1), E29–E34. <https://doi.org/10.1210/jc.2011-2132>
55. Davy, K. P., Orr, J. S. Sympathetic nervous system behavior in human obesity. *Neurosci. Biobehav. Rev.* 2009, *33* (2), 116–124. <https://doi.org/10.1016/j.neubiorev.2008.05.024>
56. Torpy JM, Lynm C, Glass RM. Chronic Stress and the Heart. *JAMA* **2007**, *298* (14), 1722. doi:10.1001/jama.298.14.1722
57. Lin, Y., Fan, R., Hao, Z., Li, J., Yang, X., Zhang, Y., Xia, Y. The Association Between Physical Activity and Insulin Level Under Different Levels of Lipid Indices and Serum Uric Acid. *Front. Physiol.* 2022, *13*, 809669. <https://doi.org/10.3389/fphys.2022.809669>
58. He, F., Li, J., Liu, Z., Chuang, C. C., Yang, W., Zuo, L. (2016). Redox Mechanism of Reactive Oxygen Species in Exercise. *Front. Physiol.* 2016, *7*, 486. <https://doi.org/10.3389/fphys.2016.00486>
59. Bracken, R. M., Brooks, S. Plasma catecholamine and nephrine responses following 7 weeks of sprint cycle training. *Amino Acids* 2010, *38* (5), 1351–1359. <https://doi.org/10.1007/s00726-009-0343-7>
60. Ziegler, M. G., Elayan, H., Milic, M., Sun, P., Gharaibeh, M. Epinephrine and the metabolic syndrome. *Curr. Hypertens. Rep.* 2012, *14* (1), 1–7. <https://doi.org/10.1007/s11906-011-0243-6>
61. Bird, S. R., Hawley, J. A. Update on the effects of physical activity on insulin sensitivity in humans. *BMJ Open Sport Exerc. Med.* 2017, *2*, e000143. <https://doi.org/10.1136/bmjsem-2016-000143>
62. Pedersen, B.K.; Saltin, B. Exercise as medicine—evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scand. J. Med. Sci. Sports* 2015, *25*, 1–72. <https://doi.org/10.1111/sms.12581>.
63. Cornelissen, V.A.; Smart, N.A. Exercise training for blood pressure: a systematic review and meta-analysis. *J. Am. Heart Assoc.* 2013, *2*, e004473. <https://doi.org/10.1161/JAHA.112.004473>
64. McEwen BS. Stress, adaptation, and disease. Allostasis and allostatic load. *Ann N Y Acad Sci.* **1998**;840:33–44. doi:10.1111/j.1749-6632.1998.tb09546.x
65. Smith, R.L.; Soeters, M.R.; Wüst, R.C.I.; Houtkooper, R.H. Metabolic Flexibility as an Adaptation to Energy Resources and Requirements in Health and Disease. *Endocr. Rev.* **2018**, *39*, 489–517. <https://doi.org/10.1210/er.2017-00211>
66. Smith, R.L.; Soeters, M.R.; Wüst, R.C.I.; Houtkooper, R.H. Metabolic Flexibility as an Adaptation to Energy Resources and Requirements in Health and Disease. *Endocr. Rev.* **2018**, *39*, 489–517. <https://doi.org/10.1210/er.2017-00211>
67. Warburton, D.E.R.; Bredin, S.S.D. Health Benefits of Physical Activity: A Systematic Review of Current Systematic Reviews. *Curr. Opin. Cardiol.* **2017**, *32*, 541–556. <https://doi.org/10.1097/HCO.0000000000000437>
68. Barnett, M. J., Doroudgar, S., Khosraviani, V., Ip, E. J. Multiple comparisons: To compare or not to compare, that is the question. *Res. Soc. Adm. Pharm.* 2022, *18* (2), 2331–2334. <https://doi.org/10.1016/j.sapharm.2021.07.006>

69. McNeil, J.; Crandell, J.; Agboola, A.; Thorpe, J.; Ward, D. S.; Girdler, S. S.; Strogatz, D.; Smith-Edwards, S.; Lightfoot, A.; Adair, L.; et al. Sleep, Health Outcomes and Body Weight (SHOW) study: a measurement burst design study on sleep and risk factors for obesity in black emerging adults in North Carolina, USA. *BMJ Open* **2024**, *14*, e087950.
70. Roelfsema, F., van Heemst, D., Iranmanesh, A., Takahashi, P., Yang, R., Veldhuis, J. D. Impact of age, sex and body mass index on cortisol secretion in 143 healthy adults. *Endocr. Connect.* 2017, *6* (7), 500–509. <https://doi.org/10.1530/EC-17-0160>
71. El-Farhan, N., Rees, D. A., Evans, C. Measuring cortisol in serum, urine and saliva - are our assays good enough?. *Ann. Clin. Biochem.* 2017, *54* (3), 308–32 <https://doi.org/10.1177/0004563216687335>
72. Seeman, T. E., Singer, B. H., Rowe, J. W., Horwitz, R. I., & McEwen, B. S. (1997). Price of adaptation--allostatic load and its health consequences. MacArthur studies of successful aging. *Arch. Intern. Med.* 1997, *157* (19), 2259–2268.

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