# Sedentary behaviour is associated with heightened cardiovascular, inflammatory and cortisol reactivity to acute psychological stress

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**Abstract**

**Background**: Sedentary behaviour is a risk factor for cardiovascular disease (CVD), but the underlying mechanisms remain unclear. Exaggerated psychobiological responses to acute psychological stress increase CVD risk. Sedentary behaviour is associated with characteristics that can predict large psychobiological stress response patterns (e.g., elevated resting blood pressure and systemic inflammation), but it is currently unknown whether sedentary behaviour and stress reactivity are directly linked. The aim of this study was to examine associations between device-assessed sedentary behaviour and measures of stress reactivity.

**Methods:** Sixty-one healthy adults wore an activPAL (thigh) and ActiGraph (wrist) for seven days to measure habitual levels of sedentary behaviour (mean ± SD = 9.96 ± 1.48 hours/day) and moderate-to-vigorous physical activity (mean ± SD = 101.82 ± 42.92 minutes/day). Participants then underwent stress reactivity testing, where beat-to-beat cardiovascular (e.g., blood pressure, total peripheral resistance), inflammatory (plasma interleukin-6, leukocytes) and salivary cortisol measurements were taken in response to an 8-minute socially evaluative Paced Auditory Serial Addition Test.

**Results:** Higher volumes of daily sedentary behaviour were associated with larger stress responses for diastolic blood pressure (B=1.264, 95%CI=0.537—1.990, $p$=.005), total peripheral resistance (B=40.563, 95%CI=19.310—61.812, $p$<.001), interleukin-6 (B=0.219, 95%CI=0.109—0.329, $p$<.001) and cortisol (B=1.844, 95%CI=1.139—2.549, $p$<.001). These findings emerged independent of *a priori* determined covariates, including daily levels of moderate-to-vigorous physical activity and adiposity.

**Discussion:** Exaggerated stress reactivity is characteristic of high sedentary behaviour and could be a novel mechanism linking sedentary behaviour with CVD. Future work should examine the impact of reducing sedentary behaviour on measures of stress reactivity, as this may have clinical relevance for preventing CVD.

**Keywords:** Sedentary behaviour; movement behaviours; sitting; stress reactivity; acute psychological stress; stress response.

## 1. Introduction

Cardiovascular disease (CVD) continues to be a major global burden and was implicated in a loss of 393 million disability-adjusted life-years in 2019 (Vos et al., 2020). Sedentary behaviour, defined as "any waking behaviour characterized by an energy expenditure ≤1.5 metabolic equivalents (METs), while in a sitting, reclining or lying posture" (Tremblay et al., 2017, p. 9), is an important CVD risk factor (Bailey et al., 2019; Patterson et al., 2018). However, the underlying mechanisms linking sedentary behaviour and CVD remain unclear (Dempsey et al., 2018). Given that adults engage in high quantities of sedentary behaviour (9.3 hours/day for British Adults) (Hamer et al., 2020), it is important to develop our understanding of these mechanisms, so that specific interventions can be established to prevent CVD.

Large psychobiological responses to acute psychological stress can trigger adverse cardiovascular events (Steptoe and Kivimäki, 2012), and when ignited regularly over time increase the risk of CVD mortality/incidence (Turner et al., 2020). Importantly, sedentary behaviour is associated higher resting levels of blood pressure (Lee and Wong, 2015), systemic inflammation (Parsons et al., 2017), and cortisol (Gubelmann et al., 2018). Elevations of these characteristics at rest have been associated with exaggerated psychobiological stress response patterns (Kidd et al., 2014; Lockwood et al., 2016; Sheffield et al., 1997; Steptoe et al., 2016). Consequently, it is biologically plausible that sedentary behaviour will relate to exaggerated stress reactivity, and if so, this may be a novel mechanism linking sedentary behaviour with CVD.

Research attempting to investigate sedentary behaviour in the context of stress reactivity has thus far yielded mixed results. Observational work has shown that "sedentary" individuals (relative to those who are physically active) have similar cardiovascular stress reactivity (Dziembowska et al., 2019; Ferreira-Silva et al., 2018), heightened heart rate during recovery from stress (Zaffalon Júnior et al., 2018), or lowered salivary cortisol stress responses (Dziembowska et al., 2019). An intervention study revealed that replacing structured/unstructured physical activity with

sedentariness over 14 days did not impact measures of stress reactivity (blood pressure, heart rate, cortisol, or interleukin-6 responses) relative to a 14 day "normal lifestyle" condition (Endrighi et al., 2016). However, this pre-existing sedentary behaviour-stress reactivity literature has relied on physical inactivity or the absence of movement as proxies for sedentary behaviour. Importantly, sedentary behaviour has postural components reflecting a unique and independent behaviour (Tremblay et al., 2017). For example, individuals can be both highly active and sedentary if they meet daily physical activity guidelines yet sit for much of the remainder of the day (Hamer et al., 2020). This is important because postural elements of sedentary behaviour are highly deleterious for resting levels of blood pressure, systemic inflammation, and cortisol (Dempsey et al., 2018; Edwardson et al., 2020; Pongratz and Straub, 2014; Thayer and Sternberg, 2006), and as mentioned above, these parameters are associated with psychobiological reactivity to stress.

The aim of this study was to directly examine the link between sedentary behaviour (defined from postural components) and psychobiological responses to stress. We hypothesised that sedentary behaviour would be associated with heightened cardiovascular (e.g., blood pressure, heart rate, total peripheral resistance), inflammatory (e.g., interleukin-6, total leukocyte count) and cortisol stress reactivity.

## 2. Material and methods

### 2.1 Participants

Sixty-one healthy adults (aged 18-60 years) were recruited via social media or word of mouth between May 2019 and December 2020. A power analysis (G*Power, Dusseldorf, Germany) revealed that a minimum sample size of 54 participants would be required to detect small effects across multisystem stress responses ($f^2$=0.2; anticipated from previous literature; Dziembowska et al., 2019), when power was set at 0.9 and alpha at 0.05. Our exclusion criteria included: a present or previously diagnosed medical condition (e.g., cardiovascular disease, depression, asthma), current acute illness, taking regular prescription medication (excluding oral contraceptives),

smokers/previous smokers (including vaping), resting systolic blood pressure >140 mmHg, and body fat percentage >32% (male) or >45% (female). Prior to arrival at the laboratory, participants abstained from over-the-counter medication for 7d, moderate-to-vigorous exercise for 24h, alcohol for 12h, drinking anything apart from water for 4h and food for 2h. All participants gave informed consent and ethical approval was granted by Loughborough University's Ethics Sub-Committee (R19-P011). This work was conducted in line with the Code of Ethics of the World Medical Association (Declaration of Helsinki; human experiments).

**2.2 Procedure**

This cross-sectional observational study consisted of two sessions. Session one was a screening session to check eligibility, and involved obtaining informed consent, brachial blood pressure measurements (Omron M6 comfort, Omron Healthcare, Milton Keynes, UK) and administering questionnaires to collect socio-demographic data, including: age, sex, ethnicity, socio-economic status (based on the head of household's current or most recent occupation), and familial (biological parent or sibling) history of cardiometabolic disease (hypertension, type 2 diabetes or cardiovascular disease). Participants were also fitted with devices to measure habitual levels of sedentary behaviour and physical activity across the following week (see below).

After seven days participants completed session two, involving a stress reactivity protocol (see Figure 1). This was conducted in a light and temperature (20–22°C) controlled laboratory, starting between 1pm and 2pm to account for diurnal variations in our outcome measures. First, height (274 stadiometer, Seca, Hamburg, Germany), weight and body fat percentage (mBCA 515 bioimpedance scales, Seca, Hamburg, Germany) measurements were taken and the 14-item Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) was completed. After all relevant equipment was attached, participants rested in a comfortable chair (in which they remained in throughout) during a 20-minute baseline period, followed by an 8-minute stress task and 45-minute recovery period. After each period participants self-reported (Likert scale; 0-7) levels of stress, engagement, difficulty, arousal, and perceived performance, with higher scores denoting greater levels (e.g., Paine

et al., 2014). Participants quietly watched a nature documentary (Planet Earth 2 or Blue Planet; BBC, UK) when data were not being recorded, in line with our previous work (Paine et al., 2014, 2013a). Any scenes/episodes that were considered arousing were avoided.

**2.3 Measures**

***2.3.1 activPAL measured sedentary behaviour***

A gold-standard 20hz activPAL3 micro inclinometer (PAL Technologies Ltd, Glasgow, UK) was waterproofed in a nitrile sleeve and attached to the middle-anterior line of the non-dominant thigh using Hypafix dressing (BSN Medical, Hamburg, Germany). The device recorded data from the first midnight after deployment for seven full continuous days (24 hours/day). Participants were asked not to take the monitor off until the recording period had concluded, but if reattachment was necessary (e.g., if the monitor was falling off), then participants were given detailed instructions of how to do this and were assisted by the research team. The activPAL utilises a proprietary algorithm (Intelligent Activity Classification), and data regarding thigh position and overall acceleration to determine postural and metabolic components of sedentary behaviour. The monitor defines sedentary behaviour as a sitting or lying posture (thigh angle <20 degrees above or below the horizontal plane) with a MET of 1.25. Research has demonstrated near perfect agreement between sedentary behaviour volume derived from the activPAL and direct observation (Edwardson et al., 2016; Kim et al., 2015). Data were analysed using validated software (Processing PAL version 1.3, Leicester, UK) which has been described elsewhere (Winkler et al., 2016). To be included in analyses, participants were required to have ≥one valid weekend day, and ≥ three weekdays, of valid data, with a valid day of data defined as >499 steps, <95% of time in any one posture and ≥10 hours of wear time (Edwardson et al., 2017). Participants were also asked to complete a seven-day log diary to measure sleep and wake times, which was combined with heatmaps to cross-reference algorithm-produced data. Any clear errors (e.g., a nap was reported but coded by the activPAL as a sedentary bout lasting the same duration) were manually corrected (Edwardson et al., 2017).

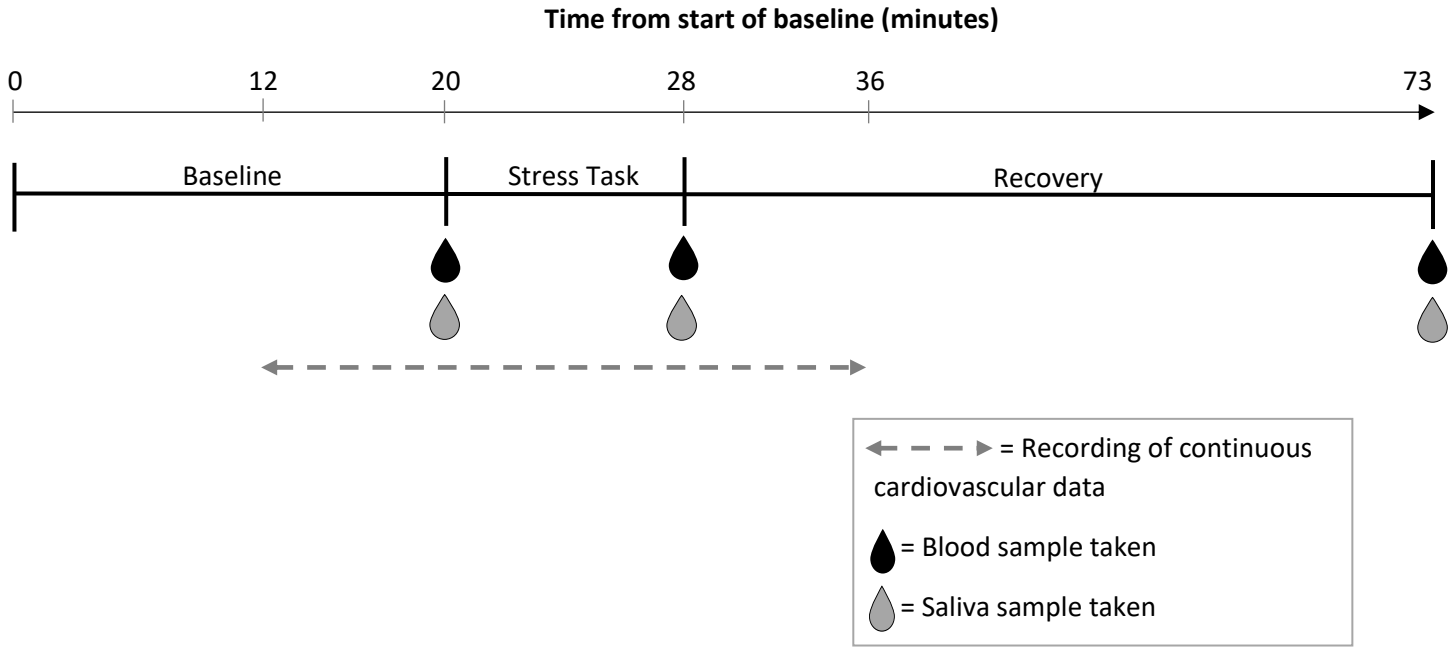


**Figure 1.** Schematic depicting the stress reactivity session.

### *2.3.2 ActiGraph measured physical activity*

Participants wore a triaxial accelerometer (ActiGraph GT3X BT+, ActiGraph, Florida, USA) on the non-dominant wrist for seven full days and nights (excluding during swimming/bathing) (e.g., Mikkelsen et al., 2020) to measure all incidental physical activity. However, due to missing sleep time stamps on the final day of recording, a maximum of six days of data were usable. Each device was set to record data at 100 Hz using ActiLife version 6 (ActiGraph, Florida, USA) and our validation criteria was defined as 16 hours of wear time per day for four valid days. Data were analysed with the R-package "GGIR" (version 2.0), which has been extensively used and detailed elsewhere (Migueles et al., 2019). Importantly, GGIR utilises raw acceleration instead of accelerometer "brand specific" cut points which enhances cross-study and cross-device comparability (Migueles et al., 2019). Moderate-vigorous physical activity (MVPA) was defined by raw acceleration >100 milli-g [mg] (Hildebrand et al., 2014).

### *2.3.3 Acute psychological stress task*

Participants completed an 8-minute version of the Paced Auditory Serial Addition Test (PASAT) (Gronwall, 1977), which reliably perturbs multisystem physiology (e.g., Veldhuijzen Van Zanten, Ring, Carroll, & Kitas, 2005). This active psychological stressor involves adding and remembering consecutive numbers, and our protocol has been described previously, including socio-evaluative elements of scoring, competition, rewards, and video-recording (Paine et al., 2013b, 2014). Participants provided answers non-verbally by pointing to a number on a sheet of paper and were awarded one point for every correct answer.

## 2.4. Physiological measures

### *2.4.1 Continuous cardiovascular activity*

Beat-to-beat systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), stroke volume (SV), cardiac output (CO) and total peripheral resistance (TPR), were measured during 8 minute blocks (the final 8 minutes of baseline, the PASAT, and the first 8 minutes of recovery) using the Human Non-Invasive Blood Pressure (NIBP) system (ADInstruments, Oxford, UK)

with Modelflow algorithms (Wesseling et al., 1993). Briefly, cardiovascular stress responses were determined based on changes in arterial diameter detected via a photoplethysmographic cuff placed on the middle phalanx of the middle finger (maintained at heart level in a heated blanket) to the contralateral limb housing a cannula. This technique meets validation criteria to accurately measure cardiovascular function (Imholz et al., 1998; Schutte et al., 2004) and is widely used in psychophysiological research (Paine et al., 2013b, 2014).

Three lead electrocardiography (ECG) measured heart rate (HR), with bipolar silver-silver chloride electrodes placed on the left and right clavicle and lower left rib. An analogue-digital converter (PowerLab, ADInstruments, Oxford, UK) sampled data at 200hz, and this data was analysed by LabChart version 8 (ADInstruments, Oxford, UK). R waves were detected automatically but the ECG trace was also manually inspected, including the removal of any missed ectopic beats.

#### *2.4.2 Blood sampling and analysis*

A 20-gauge cannula (BD Nexiva, BD, New Jersey, USA) was inserted into a suitable antecubital vein and blood was collected at the end of baseline, immediately post-stress and 45-minutes post-stress, as per others (e.g., Brydon and Steptoe, 2005). During each draw the first 2ml were discarded and then 4.7ml were collected in potassium ethylene diaminetetraacetic acid ($K_3$EDTA) evacuated blood collection tubes (Starstedt, Leicester, UK). Post-draw, the cannula was flushed with 5cc infusion saline (0.9% NaCl) to maintain patency. A 20µl sample of whole blood was analysed by a Yumizen H500 automated cell counter (Horiba Medical, Montpellier, France) to determine total and differential (neutrophil, lymphocyte, monocyte) leukocyte counts. The remainder of each sample were temporarily placed on ice for a maximum of 20 minutes and then centrifuged (2500rpm for 10 min at 4$^{o}$C) before the plasma supernatant was aliquoted and stored in Eppendorf tubes (Starstedt, Leicester, UK) at -80$^{o}$C. Interleukin-6 (IL-6) was assayed in duplicate using a high-sensitivity ELISA (R&D systems, Minneapolis, USA) in line with the manufacturer's instructions. The intra- and inter-assay coefficients of variation were 6.37% and 6.03%, respectively.

### *2.4.3 Saliva sampling and analysis*

Whole saliva was obtained (end of baseline, 8-minutes post-stress, 45-minutes post-stress) using the gold standard passive drool method. Participants swallowed the contents of their mouth and then tilted their head towards the ground twice for 60 seconds, before depositing their pooled saliva into a polypropylene vial through a SalivaBio Collection Aid (Salimetrics, California, USA). Samples were stored on ice and frozen at -80$^{o}$C after each testing session. Cortisol was assayed in duplicate using a high sensitivity enzyme immunoassay kit (Salimetrics, California, USA) with adherence to the manufacturer's instructions. The intra- and inter-assay coefficients of variation were 9.21% and 7.14%, respectively.

## 2.5 Data reduction and statistical analyses

Data were analysed using SPSS version 27 (IBM, Chicago, USA), with statistical significance set as $p < .05$. There were some missing blood (n=13 participants; cannulation difficulties) and ECG HR (n=1 participant; equipment failure) data.

Generalized estimating equations (GEE) with an autoregressive [AR(1)] correlation structure were used to analyse our repeated measure data, with appropriate distribution and link selection (e.g., gamma distribution with log link for variables with positively skewed residuals). Favourably, this approach corrects for dependency within repeated measures. The effect of time (mean of each period of baseline, stress and recovery) and time-by-group interactions were assessed, with group reflecting tertiles of activPAL-determined sedentary behaviour volume per other research (Hamer et al., 2020). These consisted of [1] low (6.62—9 hours/day; n=15), [2] medium (9—11.5 hours/day; n=38) and [3] high (11.5—13.88 hours/day, n=8) levels of daily sedentary behaviour. Wald Chi-Square with Cramér's V (*V)* as an index of effect size; *V*=0.1 (small effect), *V*=0.3 (medium effect), *V*=0.5 (large effect) are presented. Parameters showing significant time-by-condition interactions were interrogated with GEE-integrated post-hoc analyses, whereby psychobiological data at baseline, stress and recovery were compared across sedentary behaviour tertiles. The Holm-

Bonferroni correction adjusted for multiple comparisons (Holm, 1979), but unadjusted *p* values are also presented.

Generalized linear models (GLM) examined the relationship between (continuous) daily hours of sedentary behaviour and magnitude of physiological change (Δ) in response to stress, computed as 1) the difference between mean baseline and mean stress (cardiovascular variables), 2) the difference between baseline and immediately post-stress/45-minute post-stress samples (inflammatory markers) and 3) the difference between baseline and 8-minute post-stress/45-minute post-stress samples (cortisol). As above, log links were applied where appropriate to positively skewed variables. Unstandardized B-coefficients (reflecting effect size) with 95% Wald confidence intervals are displayed. The Holm-Bonferroni correction (Holm, 1979) was used to adjust for multiple GLM testing, but unadjusted *p* values are also presented.

The two generalized statistical approaches above were selected to handle any random missing data, as well as non-normally distributed variables without raw data transformation. Analyses were adjusted for the following covariates, which were selected *a priori* based on existing literature: age, sex, body fat %, activPAL waking wear time, daily minutes of MVPA, HADS depression, HADS anxiety, and the presence of cardiometabolic family disease history (Hamer et al., 2020; Steptoe et al., 2016; Turner et al., 2020). However, due to the possibility of overfitting, GLM and GEE models which included a fewer number of covariates can be found in Supplementary Material, along with associations between sedentary behaviour, psychobiological stress reactivity change scores, and our covariates. Finally, psychobiological values under baseline conditions were also included in GLMs assessing magnitude of stress reactivity (Steptoe et al., 2016; Turner et al., 2020).

## 3. Results

### 3.1 Sample characteristics

Table 1 summarises participant characteristics. Our sample consisted of mainly white young adults with body fat levels ranging from low to high. There was good compliance with the activPAL/ActiGraph wear protocols, as well as high volumes of daily sedentary behaviour and MVPA

which align with national estimates derived from similar measurement approaches (Hamer et al., 2020; Ramakrishnan et al., 2021).

**Table 1.** Sample characteristics

| | Mean (SD) / N (%) | Range (min-max) |
|---|---|---|
| ***Sociodemographic and anthropometric data*** | | |
| Age (years) | 25.69 (8.86) | 18—59 |
| Sex (female) | 32 (52.50) | N/A |
| Body mass index (kg/m$^2$) | 24.4 (4.15) | 18.7—34.60 |
| Body fat (%) | 25.47 (9.64) | 8.40—43.70 |
| Presence of family cardiometabolic disease history (yes) | 30 (49.20) | N/A |
| Ethnicity (white) | 50 (82.00) | N/A |
| A non-manual occupation category for the head of the household | 39 (63.90) | N/A |
| PASAT performance score (from 0 to 281) | 100.51 (36.11) | 35—183 |
| ***Sedentary behaviour data (activPAL)*** | | |
| Average daily hours of sedentary behaviour | 9.96 (1.48) | 6.62—13.88 |
| Average number of valid days that the activPAL was worn | 6.69 (0.22) | 4—7 |
| Average daily waking hours that the activPAL was worn | 15.18 (1.07) | 12.75—17.28 |
| ***Physical activity data (ActiGraph)*** | | |
| Average daily minutes of MVPA (ActiGraph) | 101.82 (42.92) | 27.65—235.40 |
| Average number of valid days that the ActiGraph was worn | 5.79 (0.52) | 4—6 |
| Average daily waking hours that the ActiGraph was worn | 15.90 (0.94) | 13.38—18.45 |
| ***Psychological data*** | | |
| HADS depression subscale score (from 0 to 21) | 2.18 (1.98) | 0—10 |
| HADS anxiety subscale score (from 0 to 21) | 5.43 (3.19) | 0—14 |

*Note.* PASAT=Paced Auditory Serial Addition Test, MVPA=moderate-vigorous physical activity, HADS=Hospital Anxiety and Depression Scale. Larger scores on HADS indicates greater symptoms of depression or anxiety.

### 3.2 Psychophysiological responses to the stress task

Our PASAT protocol induced a range of psychophysiological responses (see Table 2). As expected, cardiovascular (e.g., SBP, DBP, HR, CO), inflammatory (e.g., IL-6, total leukocyte count) and neuroendocrine (cortisol) markers increased in response to stress ($p$'s < .05). Participants self-reported the PASAT as stressful, engaging, arousing and difficult, and did not think they performed well ($p$'s < .05).

### *3.3 Sedentary behaviour and cardiovascular responses to stress*

GLMs assessed the relationship between hours of daily sedentary behaviour and magnitude of baseline to stress changes in cardiovascular activity (see Table 3). These revealed positive associations for DBP (B=1.264, 95% CI=0.537 — 1.990, unadjusted *p*=.001, adjusted *p*=.005) and TPR (B=40.563, 95% CI=19.310 — 61.812, unadjusted *p*<.001, adjusted *p*<.001), such that higher volumes of daily sedentary behaviour were associated with larger stress responses for these parameters. Conversely, there were negative relationships between daily hours of sedentary behaviour and baseline to stress changes in SV (B=-1.534, 95% CI=-1.927 — -1.148, unadjusted *p*<.001, adjusted *p*<.001); more hours spent sedentary per day were linked to smaller SV responses. No relationships emerged for SBP or HR stress reactivity (Table 3; adjusted *p*'s > .05), and the relationships for MAP (B=1.109, 95% CI=0.131 — 2.088, unadjusted *p*=.026, adjusted *p*=.104) and CO (B=-0.926, 95% CI=-1.840 — -0.011, unadjusted *p*=.047, adjusted *p*=.141), responses were reduced after Holm-Bonferroni correction.

GEEs were used to model tertiles of sedentary behaviour volume in the context of cardiovascular activity during our stress protocol. Significant time-by-group interactions emerged for DBP (Wald $\chi^2$=12.99, *p*=.012, *V*=.19), CO (Wald $\chi^2$=13.88, *p*=.008, *V*=.20) and TPR (Wald $\chi^2$=13.50, *p*=.009, *V*=.19), with evidence of a trend for MAP (Wald $\chi^2$=9.13, *p*=.058, *V*=.16). As shown in Figure 2, none of the post-hoc comparisons across tertile for the same stress protocol phase were significant. There were no significant time-by-group interactions for SBP (Wald $\chi^2$=3.51, *p*=.477, *V*=.10), HR (Wald $\chi^2$=2.24, *p*=.691, *V*=.08) or SV (Wald $\chi^2$=6.26, *p*=.181, *V*=.13).

**Table 2.** Psychophysiological responses to the Paced Auditory Serial Addition Test (PASAT).

| | Baseline | Stress (PASAT) | Recovery | Wald $\chi^2$ | *p* | Effect size (*V*) |
|---|---|---|---|---|---|---|
| **Cardiovascular responses** | | | | | | |
| Systolic blood pressure (mmHg) | 114.27 ± 1.56 | 135.04 ± 2.29* | 122.59 ± 1.75†* | 155.92 | **<.001** | 0.65 |
| Diastolic blood pressure (mmHg) | 58.78 ± 1.10 | 72.67 ± 1.38* | 64.66 ± 1.18†* | 277.38 | **<.001** | 0.87 |
| Mean arterial pressure (mmHg) | 75.40 ± 1.13 | 92.59 ± 1.56* | 82.21 ± 1.24†* | 262.16 | **<.001** | 0.85 |
| Heart rate (bpm) | 70.59 ± 1.32 | 80.65 ± 1.65* | 71.23 ± 1.35† | 140.83 | **<.001** | 0.63 |
| Stroke volume (ml) | 77.95 ± 2.79 | 75.36 ± 2.85 | 74.98 ± 2.91 | 5.43 | .066 | 0.12 |
| Cardiac output (l/min) | 5.47 ± 0.19 | 6.10 ± 0.25* | 5.30 ± 0.19† | 28.10 | **<.001** | 0.28 |
| Total peripheral resistance (dynes-s/cm$^{-5}$) | 1103.39 ± 31.60 | 1029.04 ± 36.25* | 1134.01 ± 34.22† | 32.90 | **<.001** | 0.30 |
| **Inflammatory responses** | | | | | | |
| Interleukin 6 (pg/ml) | 0.79 ± 0.08 | 1.04 ± 0.15* | 1.47 ± 0.14†* | 49.81 | **<.001** | 0.42 |
| Total leukocyte count ($10^9$/l) | 5.94 ± 0.24 | 6.37 ± 0.24* | 6.69 ± 0.30* | 56.08 | **<.001** | 0.44 |
| Neutrophil count ($10^9$/l) | 3.52 ± 0.19 | 3.80 ± 0.21* | 4.16 ± 0.27†* | 35.19 | **<.001** | 0.35 |
| Lymphocyte count ($10^9$/l) | 1.72 ± 0.06 | 1.83 ± 0.07* | 1.82 ± 0.06* | 14.77 | **.001** | 0.22 |
| Monocyte count ($10^9$/l) | 0.45 ± 0.02 | 0.47 ± 0.02 | 0.46 ± 0.02 | 2.60 | .272 | 0.09 |
| **Neuroendocrine responses** | | | | | | |
| Cortisol (nmol/l) | 7.17 ± 1.11 | 10.08 ± 1.82* | 6.47 ± 1.06† | 25.64 | **<.001** | 0.26 |
| **Self-reported psychological responses** | | | | | | |
| Stress (from 0 to 7) | 0.61 ± 0.11 | 4.49 ± 0.16* | 0.38 ± 0.09† | 549.33 | **<.001** | 0.89 |
| Engagement (from 0 to 7) | 2.61 ± 0.22 | 4.30 ± 0.16* | 2.43 ± 0.20† | 82.40 | **<.001** | 0.47 |
| Difficulty (from 0 to 7) | 0.98 ± 0.16 | 4.90 ± 0.12* | 0.48 ± 0.11†* | 864.07 | **<.001** | 0.91 |
| Arousal (from 0 to 7) | 1.34 ± 0.19 | 2.97 ± 0.19* | 1.30 ± 0.17† | 63.04 | **<.001** | 0.42 |
| Perceived performance (from 0 to 7) | 3.92 ± 0.19 | 1.49 ± 0.14* | 4.38 ±0.17†* | 176.71 | **<.001** | 0.69 |

*Note.* Data presented as mean ± standard error. *=significantly different from baseline, †=significantly different from stress ($p < .05$). *V*= Cramér's *V* effect size. Bold type indicates statistical significance ($p < .05$). For self-reported psychological responses, higher scores denote greater levels.

### *3.4 Sedentary behaviour and inflammatory responses to stress*

GLMs explored associations between hours of daily sedentary behaviour and magnitude of baseline to immediately post-stress inflammatory responses. There was a positive association for total leukocyte (B=-0.400, 95% CI=-0.665 — -0.135, unadjusted *p*=.003, adjusted *p*=.012) and neutrophil (B=-0.799, 95% CI=-1.311 — -0.286, unadjusted *p*=.002, adjusted *p*=.010) count changes, and no association for monocyte or lymphocyte count changes (adjusted *p*'s > .05). There was a positive association between daily hours of sedentary behaviour and the baseline to immediately post-stress IL-6 response, but this was attenuated after multiple testing correction (B=0.073, 95% CI=0.009 — 0.138, unadjusted *p*=.025, adjusted *p*=.075). In terms of baseline to 45min post-stress changes, there were positive associations for IL-6 (B=0.219, 95% CI=0.109 — 0.329, unadjusted *p*<.001, adjusted *p*<.001) and total leukocyte count (B=0.198, 95% CI=0.062 — 0.333, unadjusted *p*=.004, adjusted *p*=.020) responses. There were no relationships for neutrophil, lymphocyte, or monocyte count changes (see Table 4; adjusted *p*'s > .05).

In the GEE models, there were no significant time-by-group interactions for IL-6 (Wald $\chi^2$ = 5.95, *p*=.203, *V*=.14), total leukocyte count (Wald $\chi^2$=2.69, *p*=.611, *V*=.10), neutrophil count (Wald $\chi^2$=5.36, *p*=.253, *V*=.14), or monocyte count (Wald $\chi^2$=3.37, *p*=.499, *V*=.11). As displayed in Figure 3, there was evidence of a trend interaction for lymphocyte count (Wald $\chi^2$=9.19, *p*=.057, *V*=.18).

### *3.5 Sedentary behaviour and cortisol responses to stress*

GLMs revealed a positive association between hours of daily sedentary behaviour and the baseline to 8min post-stress change (B=1.844, 95% CI=1.139 — 2.549, unadjusted *p*<.001, adjusted *p*<.001) and baseline to 45-min post-stress change (B=0.875, 95% CI=0.334 — 1.417, unadjusted *p*=.002, adjusted *p*=.012) in cortisol, such that higher volumes of sedentary behaviour were related to larger cortisol reactivity. There was no GEE time-by-group interaction for cortisol (Wald $\chi^2$=5.65, *p*=.227, *V*=.12), which suggests that cortisol concentrations during the stress protocol did not differ in the context of our sedentary behaviour tertiles (Figure 3).

**Table 3.** Associations between daily hours of sedentary behaviour and magnitude of cardiovascular responses to stress.

| | B | Std. error | 95% Wald confidence interval | | $p^a$ | $p^b$ |
|---|---|---|---|---|---|---|
| | | | Lower | Upper | | |
| ***Cardiovascular responses from baseline to stress*** | | | | | | |
| Δ Systolic blood pressure | 0.742 | 0.81 | -0.849 | 2.322 | .358 | .716 |
| Δ Diastolic blood pressure | **1.264** | 0.37 | 0.537 | 1.990 | **.001** | **.005** |
| Δ Mean arterial pressure | 1.048 | 0.50 | 0.060 | 2.037 | .026 | .104 |
| Δ Heart rate | 0.016 | 0.04 | -0.063 | 0.094 | .698 | .716 |
| Δ Stroke volume | **-1.534** | 0.20 | -1.927 | -1.148 | **<.001** | **<.001** |
| Δ Cardiac output | -0.926 | 0.47 | -1.840 | -0.011 | .047 | .141 |
| Δ Total peripheral resistance | **40.563** | 10.84 | 19.310 | 61.812 | **<.001** | **<.001** |

Note. $p^a$ = unadjusted *p* value, $p^b$ = adjusted *p* value (Holm-Bonferroni corrected for multiple testing). GLM analyses are adjusted for covariates (age, sex, body fat %, activPAL waking wear time, daily minutes of moderate-vigorous physical activity, HADS depression, HADS anxiety, family cardiometabolic disease history, baseline cardiovascular physiology) and presented as individual effects rather than one combined model. Bold type indicates statistical significance (adjusted $p < .05$).

**Table 4.** Associations between daily hours of sedentary behaviour and magnitude of inflammatory and cortisol responses to stress.

| | B | Std. error | 95% Wald confidence interval | | $p^a$ | $p^b$ |
|---|---|---|---|---|---|---|
| | | | Lower | Upper | | |
| ***Inflammatory responses from baseline to immediately post-stress*** | | | | | | |
| Δ Interleukin 6 | 0.073 | 0.03 | 0.009 | 0.138 | .025 | .075 |
| Δ Total leukocytes | **-0.400** | 0.14 | -0.665 | -0.135 | **.003** | **.012** |
| Δ Neutrophils | **-0.799** | 0.26 | -1.311 | -0.286 | **.002** | **.012** |
| Δ Lymphocytes | -0.023 | 0.02 | -0.055 | 0.010 | .178 | .262 |
| Δ Monocytes | -0.006 | 0.01 | -0.013 | 0.002 | .131 | .262 |
| ***Inflammatory responses from baseline to 45 minutes post-stress*** | | | | | | |
| Δ Interleukin 6 | **0.219** | 0.06 | 0.109 | 0.329 | **<.001** | **<.001** |
| Δ Total leukocytes | **0.198** | 0.07 | 0.062 | 0.333 | **.004** | **.020** |
| Δ Neutrophils | 4.198 | 2.28 | -0.269 | 8.664 | .065 | .260 |
| Δ Lymphocytes | -0.018 | 0.01 | -0.041 | 0.005 | .122 | .366 |
| Δ Monocytes | 0.004 | 0.01 | -0.002 | 0.011 | .182 | .366 |
| ***Neuroendocrine response from baseline to immediately post-stress*** | | | | | | |
| Δ Cortisol | **1.844** | 0.36 | 1.139 | 2.549 | **<.001** | **<.001** |
| ***Neuroendocrine response from baseline to 45 minutes post-stress*** | | | | | | |
| Δ Cortisol | **0.875** | 0.28 | 0.334 | 1.417 | **.002** | **.012** |

Note. $p^a$ = unadjusted *p* value, $p^b$ = adjusted *p* value (Holm-Bonferroni corrected for multiple testing). GLM analyses are adjusted for covariates (age, sex, body fat %, activPAL waking wear time, daily minutes of moderate-vigorous physical activity, HADS depression, HADS anxiety, family cardiometabolic disease history, baseline inflammatory/cortisol physiology) and presented as individual effects rather than one combined model. Bold type indicates statistical significance (adjusted $p < .05$).

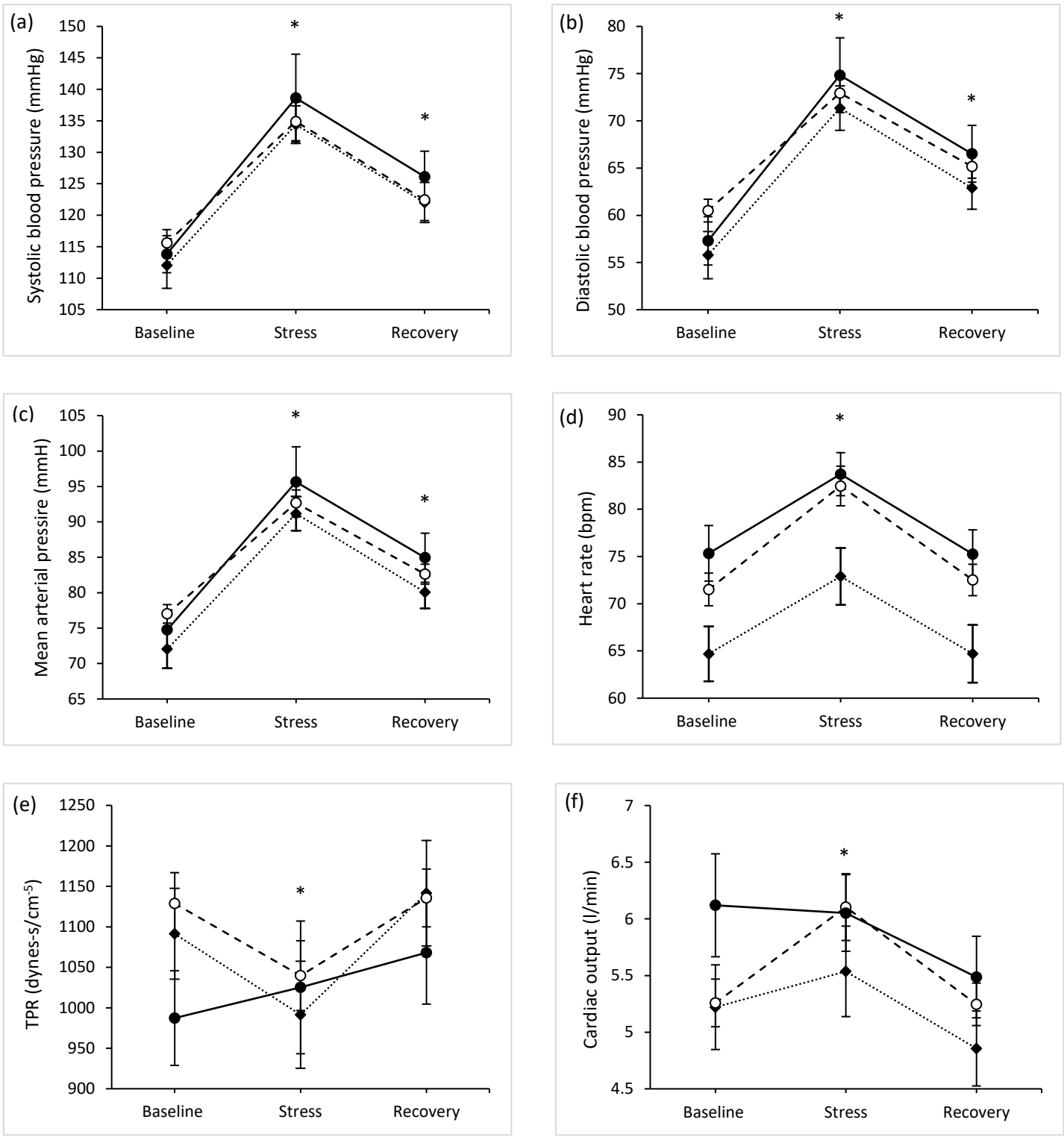


**Figure 2.** GEE time-by-group interactions for (a) systolic blood pressure, (b) diastolic blood pressure, (c) mean arterial pressure, (d) heart rate, (e) total peripheral resistance (TPR) and (f) cardiac output, with adjustment for covariates (age, sex, body fat %, activPAL waking wear time, daily minutes of moderate-vigorous physical activity, HADS depression, HADS anxiety, family cardiometabolic disease history). Data provided as estimated marginal means; error bars represent standard error of the mean. Solid line = high sedentary behaviour tertile, dashed line = medium sedentary behaviour tertile, dotted line = low sedentary behaviour tertile. * indicates significant main effect of time (different from baseline; $p < .05$).

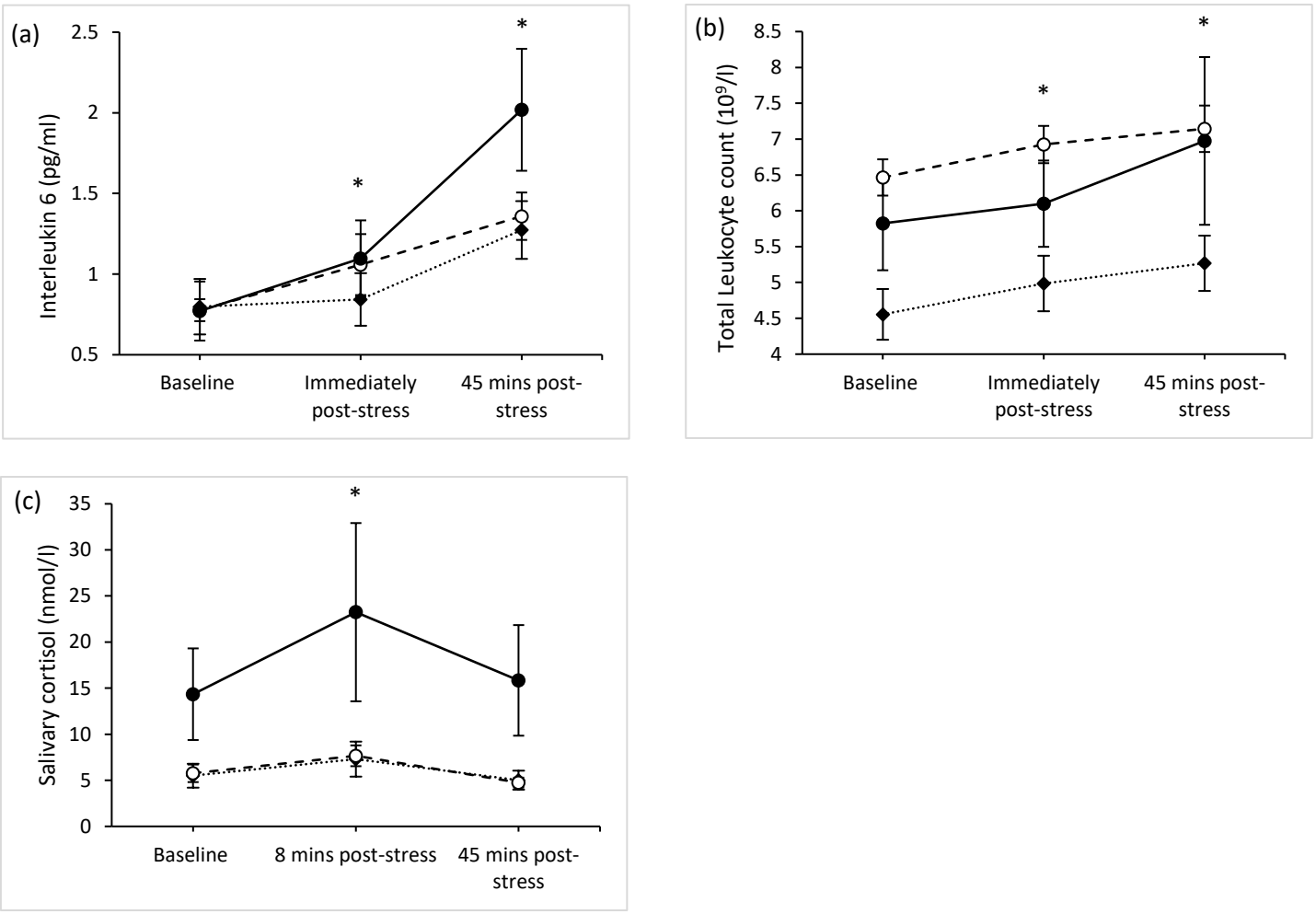


**Figure 3.** GEE time-by-group interactions for (a) interleukin-6, (b) total leukocyte count and (c) salivary cortisol, with adjustment for covariates (age, sex, body fat %, activPAL waking wear time, daily minutes of moderate-vigorous physical activity, HADS depression, HADS anxiety, family cardiometabolic disease history). Data provided as estimated marginal means; error bars represent standard error of the mean. Solid line = high sedentary behaviour tertile, dashed line = medium sedentary behaviour tertile, dotted line = low sedentary behaviour tertile. * indicates significant main effect of time (different from baseline; $p < .05$).

## 4. Discussion

Sedentary behaviour is a risk factor for CVD, but the underlying mechanisms are unclear. Dysregulated psychobiological reactivity to acute psychological stress is a physiologically plausible mechanism. This is the first study to examine whether device-assessed sedentary behaviour (including postural components as per the accepted definition; Tremblay et al., 2017) is associated with psychobiological stress responses. Higher volumes of daily sedentary behaviour were related to larger cardiovascular (DBP and TPR), inflammatory (IL-6 and total leukocyte count) and cortisol responses to stress, even after adjustment for daily MVPA levels and adiposity. Exaggerated stress reactivity might be a novel mechanism linking sedentary behaviour and CVD.

### 4.1 Sedentary behaviour and cardiovascular responses to stress

Higher volumes of daily sedentary behaviour were related to larger DBP responses to stress, possibly via increases in sympathetic activity, vagal withdrawal and vascular resistance under rest and stress (Brindle et al., 2014; Dempsey et al., 2018; Ferreira-Silva et al., 2018). Heightened beta-adrenergic receptor sensitivity in the vasculature, blood pooling and elevated hydrostatic pressure are also likely to be important mechanisms, as well as reductions in shear stress (Dempsey et al., 2018). For example, low shear stress due to the absence of muscular contraction inhibits the production of nitric oxide from the endothelium, which is critical for good vasculature health (Dyakova et al., 2015).

Our findings are clinically important, as larger DBP responses to stress are prospectively associated with hypertension, CVD incidence (Turner et al., 2020) and CVD mortality (Carroll et al., 2012). Consequently, our findings may also reflect a novel mechanism from sedentary behaviour to CVD, potentially because large DBP stress reactivity signals early physiological dysregulation that has not yet surfaced as clinically relevant under resting conditions, but over time develops into CVD (Turner et al., 2020; Zaffalon Júnior et al., 2018). Further, as DBP responses to laboratory-induced psychological stress reflect DBP responses to everyday life stressors (Kamarck et al., 2003), an exaggerated DBP stress response profile ignited regularly over time is a plausible CVD mechanism

(Turner et al., 2020). Finally, large blood pressure responses to stress are often associated with a prothrombic state, which may precede the triggering of acute coronary events (Carroll et al., 2012; De Boer et al., 2007).

Previous research has demonstrated associations between high sedentary behaviour and elevated resting blood pressure (Dempsey et al., 2018; Edwardson et al., 2020; Lee and Wong, 2015). However, in contrast to our study, no relationship between sedentary behaviour and blood pressure reactivity to acute psychological stress has been shown in the literature thus far (Ferreira-Silva et al., 2018). One explanation for this discrepancy is that our study is the first to measure postural components of sedentary behaviour using a gold standard inclinometry approach. In support, others have documented relationships between sedentary behaviour and resting blood pressure only when sedentary behaviour was quantified using a similar approach to this study, rather than as a lack of movement (Edwardson et al., 2020). In the present study it is not clear why significant findings only emerged for DBP and not SBP reactivity, although others have reported links between sedentary behaviour and resting DBP, but not resting SBP (Edwardson et al., 2020). Further, resting DBP (relative to SBP) can be more reflective of CVD in young adult populations which make up the majority of our sample (Luo et al., 2020).

Our results suggest that sedentary behaviour is associated with a vascular-dominant (rather than cardiac-dominant) pattern of stress reactivity, as evidenced by positive associations with total peripheral resistance stress responses, alongside negative associations with cardiac output and stroke volume responses (Sherwood et al., 1990). This may be of clinical significance, given that greater peripheral vasoconstriction in response to stress is associated with CVD mortality (Kim et al., 2019) and implicated in mental stress-induced ischaemia with the potential to trigger acute cardiovascular events (Shah et al., 2020). In fact, blood pressure reactivity appears most deleterious for CVD when driven by primarily vascular mechanisms (Brindle et al., 2016; Turner et al., 2020). Previous research exploring the links between sedentary behaviour and vascular responses to stress is scarce, but one study has shown that sedentary individuals (compared to active) have reduced

forearm blood flow and vascular conductance under stress (i.e., indicative of an unhealthy vascular stress response pattern) (Ferreira-Silva et al., 2018). Overall, this literature should be extended with further vascular assessments (e.g., pulse wave velocity and flow mediated dilation) in response to passive stress tasks, which are known to elicit vascular-dominant stress response patterns (Sherwood et al., 1990).

**4.2 Sedentary behaviour and inflammatory responses to stress**

A positive relationship emerged between sedentary behaviour and the baseline to 45min post-stress total leukocyte response, with neutrophils appearing to drive this effect (See Table 4). As sedentary behaviour is related to lower resting shear stress (Dempsey et al., 2018) and an attenuated cardiac output response to stress (as shown in Table 3), adrenergic influence on adhesion molecules is plausibly the chief underlying mechanism (Segerstrom and Miller, 2004). The release of neutrophils from bone marrow as a result of cortisol stimulation is also a feasible contributing factor (Ronchetti et al., 2018); in support, our data revealed positive associations between changes in cortisol from baseline to immediately post-stress and the baseline to 45min post-stress neutrophil response (B=0.066, 95% CI=0.044 — 0.087, $p$<.001). However, although elevated leukocyte responses to stress likely reflect heightened levels of inflammation (Segerstrom and Miller, 2004; Willis et al., 2018), they do not indicate cell function including any altered inflammatory action of each cell.

Nevertheless, sedentary behaviour was also associated with larger IL-6 changes from baseline to immediately-post stress, with the size of this response even greater from baseline to 45min post-stress. In those with the highest volumes of sedentary behaviour, IL-6 stress responses were even of comparable magnitude to coronary artery disease patients (Sullivan et al., 2020). Consequently, this provides further evidence that sedentary behaviour is linked to a heightened pro-inflammatory stress response profile, which aligns with studies relating sedentary behaviour and inflammation at rest (Parsons et al., 2017; Willis et al., 2018). Monocytes are the major immune cell source of IL-6 (Goebel et al., 2000), but are unlikely to explain our IL-6 findings due to the short time course of our

stress protocol (Goebel et al., 2000; Marsland et al., 2017) and that monocyte cell numbers remained unperturbed in response to stress. In fact, there was also a slight negative association between daily sedentary behaviour and the baseline to immediately post-stress change in total leukocytes, possibly reflecting that leukocytes in general were not a major driving force underpinning our inflammatory findings. Instead, vascular endothelial cells could be the dominant mechanism, working primarily via enhanced stimulation of adrenergic pathways that occurs during acute psychological stress and as a consequence of excessive sedentary behaviour (Brindle et al., 2014; Dempsey et al., 2018).

Our inflammatory findings could have clinical relevance, both for CVD development and triggering of acute coronary syndromes (Marsland et al., 2017; Sullivan et al., 2020). For example, heightened inflammatory responses to stress are temporally linked to major cardiovascular events in female coronary heart disease patients (Sullivan et al., 2020), hypertension (Brydon and Steptoe, 2005; Steptoe et al., 2016) and increased carotid artery stiffness (Ellins et al., 2008). Consequently, this study may have elucidated a further pathway from sedentary behaviour to CVD outcomes (Bailey et al., 2019; Patterson et al., 2018). Interestingly, our findings were also observed notwithstanding a lack of baseline difference in inflammatory markers (see Figure 3), which may highlight the clinical applications of stress reactivity testing over and above resting assessments of systemic inflammation.

It is important to note that our results differ to a previous study (Endrighi et al., 2016). Variations in research design may offer an explanation, including that inducing modest increases in sedentary time over 14 days might be an insufficient stimulus to impact inflammatory stress response patterns, particularly in healthy and physically active individuals (Endrighi et al., 2016). In addition, this previous study was unable to induce a significant IL-6 response to stress.

**4.3 Sedentary behaviour and cortisol responses to stress**

Higher volumes of daily sedentary behaviour were related to larger baseline to 8min post-stress salivary cortisol responses to stress. As such, heightened cortisol reactivity may also help explain why sedentary behaviour confers augmented CVD risk, possibly via pathways of hypertension and coronary artery calcification (Turner et al., 2020). Hyperactivation of autonomic and inflammatory mechanisms under stress may mechanistically underpin our findings, including greater catecholaminergic activation of the hypothalamus and direct influence of IL-6 (Turnbull and Rivier, 1999). However, further research is needed to confirm this.

Although this study demonstrated a positive association between sedentary behaviour and cortisol stress responses, others have documented no link (Endrighi et al., 2016) or have even showed a lowered cortisol stress response in sedentary relative to active individuals (Dziembowska et al., 2019). Methodological differences may offer explanations, including that in the study by Dziembowska et al. (2019) saliva sampling took place in the morning, which means confounding from the cortisol awakening response is possible. Importantly, our findings align with research under resting conditions, where links between higher sedentary behaviour and elevated resting salivary cortisol concentrations have been reported (e.g., Gubelmann et al., 2018).

**4.4 Methodological considerations**

This study had many strengths, including being the first stress reactivity study to accurately measure and investigate sedentary behaviour in line with the accepted definition (Tremblay et al., 2017). Previous research has relied on physical inactivity as an index of sedentary behaviour, but we measured both postural and metabolic sedentary behaviour components using gold standard inclinometry. Secondly, the extensive range of psychobiological outcomes we assessed across many systems, including continuous assessment of cardiovascular activity rather than using intermittent techniques. Thirdly, is the use of robust generalized statistical models, which do not assume data sphericity and account for non-normally distributed and random missing data.

However, the following considerations should be taken into account. First, our sample were healthy and more physically active than we expected, which may have offered some protection against exaggerated reactivity (Mücke et al., 2018) and explain our modest effect sizes. However, our effect sizes were comparable to similar studies (Dziembowska et al., 2019; Ferreira-Silva et al., 2018), we statistically adjusted for physical activity throughout, and that significant findings still emerged potentially demonstrates the highly pervasive nature of sedentary behaviour on stress reactivity. Second, despite adjusting for important covariates our study was cross-sectional, and therefore directionality and causality cannot be determined. We included a large number of covariates to strengthen inference regarding independent associations between sedentary behaviour and stress reactivity, but it is possible that this contributed to "overfitting" and influenced our results. However, it should be noted that our findings were similar in simpler models (which only included the following covariates: age, sex, body fat % and activPAL wear time, as well as baseline physiology for GLM models; see Supplementary Material). It is also important to note that our covariates (e.g., body fat) may mediate the relationship between sedentary behaviour and psychobiological stress reactivity measures. This should be directly tested and explored in future research, as this may reveal further targets for potential intervention. Third, our extensive exclusion criteria ensured a healthy sample. Although this could be considered a strength due to a reduced likelihood of comorbid confounding, it also compromises the external validity of our findings. Fourth, due to technical difficulties we had a reduced sample size for inflammatory marker analyses, but our overall sample size is still larger than similar studies in the field (Dziembowska et al., 2019; Ferreira-Silva et al., 2018). A modest sample size may also help explain the discrepancies between our GEE and GLM findings. Finally, a wider assessment of the inflammatory and vascular response to stress would have been beneficial.

**4.5 Conclusion**

Device-assessed sedentary behaviour is related to heightened multisystem (i.e., cardiovascular, inflammatory, and cortisol) stress reactivity, which may be a novel mechanism underpinning

established links between sedentary behaviour and CVD. Future research may investigate the effects of context-specific sedentary behaviours on responses to stress, including interactions with physical activity. Later work should explore whether reducing sedentary behaviour attenuates measures of stress reactivity, as this may have clinical relevance for CVD prevention.

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**Supplementary Material 1.** Bivariate correlation matrix showing associations between sedentary behaviour and our *a priori* determined continuous covariate variables.

| | Average daily hours of sedentary behaviour | Age (years) | Body fat % | Av. daily minutes of MVPA | Av. daily waking hours of activPAL wear | HADS depression score |
|---|---|---|---|---|---|---|
| Average daily hours of sedentary behaviour | — | | | | | |
| Age (years) | .077 | — | | | | |
| Body fat % | **.322*** | **.287*** | — | | | |
| Av. daily minutes of MVPA | **-.423*** | -.027 | **-.236*** | — | | |
| Av. daily waking hours of activPAL wear | **.250*** | **.272*** | .089 | **.278*** | — | |
| HADS depression score | -.084 | .094 | **.203*** | .004 | **-.153*** | — |
| HADS anxiety score | -.045 | .086 | **.297*** | -.038 | -.100 | **.493*** |

**Note:** Bold font with asterisk reflects $p < .05$. Av = average, MVPA = moderate-to-vigorous physical activity, HADS = Hospital Anxiety and Depression Scale.

**Supplementary Material 2.** Bivariate correlation matrix showing associations between cardiovascular stress reactivity change variables (from baseline to stress) and our a priori determined continuous covariate variables.

| | Δ SBP | Δ DBP | Δ MAP | Δ HR | Δ SV | Δ CO | Δ TPR | Age (years) | Body fat % | Av. daily minutes of MVPA | Av. daily waking hours of activPAL wear | HADS depression score |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Δ SBP | — | | | | | | | | | | | |
| Δ DBP | **.798*** | — | | | | | | | | | | |
| Δ MAP | **.903*** | **.937*** | — | | | | | | | | | |
| Δ HR | **.244*** | **.238*** | **.236*** | — | | | | | | | | |
| Δ SV | **-.189*** | **.238*** | **-.362*** | **.180*** | — | | | | | | | |
| Δ CO | -.079 | **-.237*** | **-.224*** | **.564*** | **.877*** | — | | | | | | |
| Δ TPR | **-.163*** | .122 | -.021 | **-.420*** | **-.560*** | **-.580*** | — | | | | | |
| Age (years) | **-.254*** | **-.343*** | **-.266*** | .127 | -.038 | -.047 | **.151*** | — | | | | |
| Body fat % | **-.254*** | **-.249*** | **-.279*** | **.174*** | .088 | **.213*** | .071 | **.287*** | — | | | |
| Av. daily minutes of MVPA | -.111 | -.066 | -.021 | -.103 | -.131 | -.138 | .050 | -.027 | **-.236*** | — | | |
| Av. daily waking hours of activPAL wear | **-.264*** | **-.272*** | **-.267*** | -.096 | -.043 | -.071 | -.020 | **272*** | .089 | **.278*** | — | |
| HADS depression score | **.187*** | .137 | **.163*** | -.016 | **-.183*** | -.133 | .125 | .094 | **.203*** | .004 | **-.153*** | — |
| HADS anxiety score | -.028 | -.082 | -.097 | -.067 | .001 | -.019 | -.041 | .086 | **.297*** | -.038 | -.038 | **.493*** |

**Note:** Bold font with asterisk reflects $p < .05$. Δ indicates changes from baseline to stress. SBP = systolic blood pressure, DBP = diastolic blood pressure, MAP= mean arterial pressure, HR = heart rate, SV = stroke volume, CO = cardiac output, TPR = total peripheral resistance, av = average, MVPA = moderate-to- vigorous physical activity, HADS = Hospital Anxiety and Depression Scale.

**Supplementary Material 3.** Bivariate correlation matrix showing associations between inflammatory and cortisol stress reactivity change variables (from baseline to stress) and our *a priori* determined continuous covariate variables.

| | Δ IL-6 | Δ Total leukocytes | Δ Neutrophils | Δ Lymphocytes | Δ Monocytes | Δ Cortisol† | Age (years) | Body fat % | Av. daily minutes of MVPA | Av. daily waking hours of activPAL wear | HADS depression score |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Δ IL-6 | — | | | | | | | | | | |
| Δ Total leukocytes | .141 | — | | | | | | | | | |
| Δ Neutrophils | .041 | **.749*** | — | | | | | | | | |
| Δ Lymphocytes | -.028 | **.503*** | .046 | — | | | | | | | |
| Δ Monocytes | .031 | **.650*** | **.362*** | **.418*** | — | | | | | | |
| Δ Cortisol† | **.411*** | -.111 | -.155 | **-.178*** | -.101 | — | | | | | |
| Age (years) | -.034 | .089 | .082 | -.109 | -.082 | .012 | — | | | | |
| Body fat % | .100 | -.107 | .158 | -.042 | -.125 | -.021 | **.287*** | — | | | |
| Av. daily minutes of MVPA | **-.199*** | .076 | .153 | -.147 | **-.198*** | .072 | -.027 | **-.236*** | — | | |
| Av. daily waking hours of activPAL wear | -.137 | -.024 | **.209*** | -.133 | -.088 | .026 | **.272*** | .089 | **.278*** | — | |
| HADS depression score | -.100 | -.145 | -.113 | **-.174*** | -.040 | .126 | .094 | **.203*** | .004 | **-.153*** | — |
| HADS anxiety score | -.188 | .070 | -.084 | -.093 | **.164*** | **-.170*** | .086 | **.297*** | -.038 | -.100 | **.493*** |

**Note:** Bold font with asterisk reflects $p < .05$. Δ indicates change from baseline to immediately post-stress, † indicates change from baseline to 8 minutes post-stress. IL-6 = Interleukin-6, Av = average, MVPA = moderate-to-vigorous physical activity, HADS = Hospital Anxiety and Depression Scale.

**Supplementary Material 4.** Bivariate correlation matrix showing associations between inflammatory and cortisol stress reactivity change variables (from baseline to recovery) and our a priori determined continuous covariate variables.

| | Δ IL-6 | Δ Total leukocytes | Δ Neutrophils | Δ Lymphocytes | Δ Monocytes | Δ Cortisol[†] | Age (years) | Body fat % | Av. daily minutes of MVPA | Av. daily waking hours of activPAL wear | HADS depression score |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Δ IL-6 | — | | | | | | | | | | |
| Δ Total leukocytes | **.330*** | — | | | | | | | | | |
| Δ Neutrophils | **.335*** | **.977*** | — | | | | | | | | |
| Δ Lymphocytes | -.107 | -.106 | **-.309*** | — | | | | | | | |
| Δ Monocytes | .033 | **.631*** | **.539*** | **.181*** | — | | | | | | |
| Δ Cortisol[†] | **.391*** | **.246*** | **.226*** | .012 | **.379*** | — | | | | | |
| Age (years) | .031 | .089 | .108 | -.117 | .012 | .087 | — | | | | |
| Body fat % | .013 | -.156 | -.077 | **-.281*** | **-.377*** | -.042 | **.287*** | — | | | |
| Av. daily minutes of MVPA | **-.198*** | .082 | .083 | .010 | -.042 | .010 | -.027 | **-.236*** | — | | |
| Av. daily waking hours of activPAL wear | **.199*** | .122 | **.194*** | **-.340*** | **-.173*** | -.056 | **.272*** | .089 | **.278*** | — | |
| HADS depression score | -.012 | .042 | .054 | -.055 | .044 | .121 | .094 | **.203*** | .004 | **-.153*** | — |
| HADS anxiety score | -.087 | -.155 | -.136 | -.073 | -.037 | .120 | .086 | **.297*** | -.038 | -.100 | **.493*** |

**Note:** Bold font with asterisk reflects $p < .05$. Δ indicates change from baseline to 45 minutes post-stress. IL-6 = Interleukin-6, Av = average, MVPA = moderate-to-vigorous physical activity, HADS = Hospital Anxiety and Depression Scale.

**Supplementary Material 5**. One-way ANOVAs assessing differences in sedentary behaviour time and psychobiological stress reactivity change scores, across our *a priori* determined categorical covariate variables.

| | **Mean** | ***SD*** |
|---|---|---|
| **Average daily hours of sedentary behaviour** | | |
| Sex (male) | 9.77 | 1.65 |
| Sex (female) | 10.13 | 1.27 |
| Family history of cardiometabolic disease (yes) | **10.19*** | 1.40 |
| Family history of cardiometabolic disease (no) | **9.74*** | 1.51 |
| **Δ Systolic blood pressure from baseline to stress (mmHg)** | | |
| Sex (male) | **25.97*** | 10.01 |
| Sex (female) | **16.06*** | 13.74 |
| Family history of cardiometabolic disease (yes) | 21.59 | 14.63 |
| Family history of cardiometabolic disease (no) | 19.98 | 11.35 |
| **Δ Diastolic blood pressure from baseline to stress (mmHg)** | | |
| Sex (male) | **16.25*** | 6.53 |
| Sex (female) | **11.74*** | 6.21 |
| Family history of cardiometabolic disease (yes) | 14.27 | 8.38 |
| Family history of cardiometabolic disease (no) | 13.51 | 4.65 |
| **Δ Mean arterial pressure from baseline to stress (mmHg)** | | |
| Sex (male) | **20.50*** | 6.68 |
| Sex (female) | **14.19*** | 8.58 |
| Family history of cardiometabolic disease (yes) | 17.87 | 9.45 |
| Family history of cardiometabolic disease (no) | 16.53 | 7.09 |
| **Δ Heart rate from baseline to stress (bpm)** | | |
| Sex (male) | **8.52*** | 5.94 |
| Sex (female) | **11.39*** | 8.47 |
| Family history of cardiometabolic disease (yes) | **7.90*** | 4.30 |
| Family history of cardiometabolic disease (no) | **12.06*** | 9.17 |
| **Δ Stroke volume from baseline to stress (ml)** | | |
| Sex (male) | -3.63 | 11.84 |
| Sex (female) | -1.66 | 16.31 |
| Family history of cardiometabolic disease (yes) | -3.65 | 13.00 |
| Family history of cardiometabolic disease (no) | -1.58 | 15.55 |
| **Δ Cardiac output from baseline to stress (l/min)** | | |
| Sex (male) | **0.35*** | 0.98 |
| Sex (female) | **0.87*** | 1.63 |
| Family history of cardiometabolic disease (yes) | **0.39*** | 0.85 |
| Family history of cardiometabolic disease (no) | **0.85*** | 1.72 |

| | | |
|---|---|---|
| **Δ Total peripheral resistance from baseline to stress (dynes-s/cm$^{-5}$)** | | |
| Sex (male) | -55.45 | 232.04 |
| Sex (female) | -91.48 | 203.11 |
| Family history of cardiometabolic disease (yes) | **-32.31*** | 170.24 |
| Family history of cardiometabolic disease (no) | **-115.03*** | 249.28 |
| **Δ Interleukin 6 from baseline to immediately post-stress (pg/ml)** | | |
| Sex (male) | 0.21 | 0.64 |
| Sex (female) | 0.28 | 0.73 |
| Family history of cardiometabolic disease (yes) | **0.43*** | 0.91 |
| Family history of cardiometabolic disease (no) | **0.05*** | 0.15 |
| **Δ Interleukin 6 from baseline to 45 minutes post-stress (pg/ml)** | | |
| Sex (male) | 0.63 | 0.69 |
| Sex (female) | 0.75 | 0.87 |
| Family history of cardiometabolic disease (yes) | **0.90*** | 0.97 |
| Family history of cardiometabolic disease (no) | **0.47*** | 0.43 |
| **Δ Total leukocyte count from baseline to immediately post-stress ($10^9$/l)** | | |
| Sex (male) | 0.45 | 0.36 |
| Sex (female) | 0.41 | 0.57 |
| Family history of cardiometabolic disease (yes) | 0.43 | 0.39 |
| Family history of cardiometabolic disease (no) | 0.44 | 0.53 |
| **Δ Total leukocyte count from baseline to 45 minutes post-stress ($10^9$/l)** | | |
| Sex (male) | 0.87 | 0.90 |
| Sex (female) | 0.62 | 1.47 |
| Family history of cardiometabolic disease (yes) | 0.80 | 1.39 |
| Family history of cardiometabolic disease (no) | 0.71 | 0.92 |
| **Δ Neutrophil count from baseline to immediately post-stress ($10^9$/l)** | | |
| Sex (male) | 0.25 | 0.37 |
| Sex (female) | 0.31 | 0.39 |
| Family history of cardiometabolic disease (yes) | 0.28 | 0.40 |
| Family history of cardiometabolic disease (no) | 0.27 | 0.37 |
| **Δ Neutrophil count from baseline to 45 minutes post-stress ($10^9$/l)** | | |
| Sex (male) | 0.65 | 0.88 |
| Sex (female) | 0.61 | 1.47 |
| Family history of cardiometabolic disease (yes) | 0.69 | 1.37 |
| Family history of cardiometabolic disease (no) | 0.57 | 0.93 |

| | | |
|---|---|---|
| **Δ Lymphocyte count from baseline to immediately post-stress ($10^9$/l)** | | |
| Sex (male) | 0.15 | 0.22 |
| Sex (female) | 0.14 | 0.19 |
| Family history of cardiometabolic disease (yes) | 0.13 | 0.20 |
| Family history of cardiometabolic disease (no) | 0.16 | 0.21 |
| **Δ Lymphocyte count from baseline to 45 minutes post-stress ($10^9$/l)** | | |
| Sex (male) | **0.16*** | 0.15 |
| Sex (female) | **0.03*** | 0.27 |
| Family history of cardiometabolic disease (yes) | 0.09 | 0.25 |
| Family history of cardiometabolic disease (no) | 0.12 | 0.19 |
| **Δ Monocyte count from baseline to immediately post-stress ($10^9$/l)** | | |
| Sex (male) | 0.02 | 0.07 |
| Sex (female) | 0.02 | 0.08 |
| Family history of cardiometabolic disease (yes) | 0.03 | 0.06 |
| Family history of cardiometabolic disease (no) | 0.01 | 0.09 |
| **Δ Monocyte count from baseline to 45 minutes post-stress ($10^9$/l)** | | |
| Sex (male) | **0.05*** | 0.05 |
| Sex (female) | **-0.02*** | 0.07 |
| Family history of cardiometabolic disease (yes) | **0.01*** | 0.08 |
| Family history of cardiometabolic disease (no) | **0.03*** | 0.06 |
| **Δ Cortisol concentration from baseline to 8 minutes post-stress (nmol/l)** | | |
| Sex (male) | **4.44*** | 8.37 |
| Sex (female) | **1.53*** | 6.41 |
| Family history of cardiometabolic disease (yes) | 3.20 | 8.11 |
| Family history of cardiometabolic disease (no) | 2.64 | 6.96 |
| **Δ Cortisol concentration from baseline to 45 minutes post-stress (nmol/l)** | | |
| Sex (male) | -0.90 | 4.56 |
| Sex (female) | -0.52 | 5.07 |
| Family history of cardiometabolic disease (yes) | -1.15 | 4.59 |
| Family history of cardiometabolic disease (no) | -0.26 | 5.03 |

**Note:** Bold font with asterisk reflects a statistically significant difference ($p < .05$) across category (e.g., males vs females or presence of family cardiometabolic disease history vs no family history of cardiometabolic disease). SD = standard deviation.

**Supplementary Material 6:** Associations between daily hours of sedentary behaviour and the magnitude of cardiovascular changes from baseline to stress with fewer covariates included in adjustment

| | B | Std. error | 95% Wald confidence interval | | $p^a$ | $p^b$ |
|---|---|---|---|---|---|---|
| | | | Lower | Upper | | |
| ***Cardiovascular responses from baseline to stress*** | | | | | | |
| Δ Systolic blood pressure | 1.075 | 0.69 | -0.287 | 2.437 | .122 | .244 |
| Δ Diastolic blood pressure | **0.988** | 0.34 | 0.321 | 1.656 | **.004** | **.024** |
| Δ Mean arterial pressure | 0.891 | 0.43 | 0.047 | 1.734 | .038 | .144 |
| Δ Heart rate | 0.026 | 0.03 | -0.035 | 0.086 | .407 | .407 |
| Δ Stroke volume | **-2.017** | 0.63 | -3.251 | -0.784 | **.001** | **.007** |
| Δ Cardiac output | -0.218 | 0.09 | -0.403 | -0.033 | .021 | .084 |
| Δ Total peripheral resistance | **26.796** | 9.71 | 7.758 | 45.834 | **.006** | **.030** |

Note. $p^a$ = unadjusted *p* value, $p^b$ = adjusted *p* value (Holm-Bonferroni corrected for multiple testing). These analyses are adjusted for covariates (age, sex, body fat %, activPAL waking wear time and the appropriate baseline cardiovascular parameter) and presented as individual effects rather than one combined model. Bold type indicates statistical significance (adjusted $p < .05$).

**Supplementary Material 7:** Associations between daily hours of sedentary behaviour and the magnitude of inflammatory and cortisol changes from baseline to stress and baseline to recovery, with fewer covariates included in adjustment

| | B | Std. error | 95% Wald confidence interval | | $p^a$ | $p^b$ |
|---|---|---|---|---|---|---|
| | | | Lower | Upper | | |
| ***Inflammatory responses from baseline to 8 minutes post-stress*** | | | | | | |
| Δ Interleukin 6 | **0.101** | 0.03 | 0.033 | 0.169 | **.003** | **.012** |
| Δ Total leukocytes | **-0.059** | 0.19 | -0.098 | -0.020 | **.003** | **.012** |
| Δ Neutrophils | **-0.202** | 0.04 | -0.286 | -0.118 | **<.001** | **<.001** |
| Δ Lymphocytes | 0.058 | 0.36 | -0.650 | 0.765 | .873 | 1.000 |
| Δ Monocytes | 0.001 | 0.01 | -0.006 | 0.007 | .844 | 1.000 |
| ***Inflammatory responses from baseline to 45 minutes post-stress*** | | | | | | |
| Δ Interleukin 6 | **0.270** | 0.06 | 0.148 | 0.391 | **<.001** | **<.001** |
| Δ Total leukocytes | **0.228** | 0.09 | 0.048 | 0.409 | **.013** | **.039** |
| Δ Neutrophils | **0.403** | 0.07 | 0.264 | 0.542 | **<.001** | **<.001** |
| Δ Lymphocytes | 0.148 | 0.10 | -0.346 | 0.050 | .143 | .192 |
| Δ Monocytes | 0.005 | 0.01 | -0.001 | 0.011 | .096 | .192 |
| ***Neuroendocrine response from baseline to 8 minutes post-stress*** | | | | | | |
| Δ Cortisol | **1.301** | 0.10 | 1.113 | 1.489 | **<.001** | **<.001** |
| ***Neuroendocrine response from baseline to 45 minutes post-stress*** | | | | | | |
| Δ Cortisol | **0.615** | 0.23 | 0.164 | 1.067 | **.008** | **.032** |

Note. $p^a$ = unadjusted *p* value, $p^b$ = adjusted *p* value (Holm-Bonferroni corrected for multiple testing). GLM analyses are adjusted for covariates (age, sex, body fat %, activPAL waking wear time and the appropriate baseline psychobiological parameter) and presented as individual effects rather than one combined model. Bold type indicates statistical significance (adjusted $p < .05$).

**Supplementary Material 8:** Generalized estimating equation models with a reduced number of covariates.

In statistical models which included only age, sex, body fat percentage and activPAL waking wear time as covariates, there were still significant time-by-group interaction effects observed for DBP (Wald $\chi^2$=12.74, *p*=.013, *V*=.13), CO (Wald $\chi^2$=12.20, *p*=.016, *V*=.13) and TPR (Wald $\chi^2$=14.93, *p*=.005, *V*=.14). There was still evidence of a trend for MAP (Wald $\chi^2$=9.09, *p*=.059, *V*=.11) and lymphocyte cell count (Wald $\chi^2$=9.38, *p*=.052, *V*=.13). There were still no significant interaction effects observed for SBP, HR, SV, IL-6 concentration, total leukocyte count, neutrophil count, monocyte count or cortisol concentration (*p*'s > .05)