Effects of Concurrent Exercise Training on Body Composition, Systemic Inflammation and Components of Metabolic Syndrome in Inactive Academics; a Randomised Controlled Trial

Key words: university staff, prevention, physical activity, endurance and resistance exercise, workplace intervention

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Trial Registration

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Conflict of interest

The authors declare no conflict of interests

Abstract

Purpose: Low physical activity in the academic workplace may increase the risk of cardiometabolic disease. This randomised controlled trial investigated the effect of 14-weeks of concurrent exercise training (CT) on components of metabolic syndrome, body composition, insulin resistance and markers of systemic inflammation in inactive academics. ***Methods:*** 59 inactive academics were randomised into a CT (n=29) or wait-list control group (n=30). CT performed supervised training at an onsite facility 3 times per week for 14 weeks and cardiometabolic health was assessed pre- and post-intervention. Aerobic capacity was measured via a metabolic cart. Dual Energy X-ray Absorptiometry measured fat mass, lean mass and central adiposity. Fasting blood samples were analysed for interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), glucose, and lipid profile. ***Results:*** Following the intervention there was a decrease in fat mass (mean±SD; -1.3±1.4%), android fat mass (median (IQR); -0.06 (0.27) kg) and visceral adipose tissue (median (IQR); -66 (110) cm^3) in CT, but not control. Lean mass (median (IQR); 1.35 (1.86) kg) and aerobic capacity (mean±SD; 4.0±3.1 mL/kg/min) increased in CT, but not in control. There were no changes in IL-6, TNF-a, HOMA-IR, glucose or lipid profile in response to the intervention (P>0.05). Changes in insulin resistance were positively associated with IL-6 in the control group only (Coefficients [95%CI]; 5.957 [2.961, 8.953]). ***Conclusion:*** Implementing combined aerobic and resistance exercise training programs in academic institutions may be an appropriate intervention to increase physical activity and reduce risk factors associated with cardiometabolic disease.

Abbreviations

ANOVA	Analysis of variance
BMI	Body mass index
CT	Concurrent Training
DBP	Diastolic blood pressure
DEXA	Dual Energy X-ray Absorptiometry
EDTA	Ethylenediaminetetraacetic acid
GLTEQ	Godin Leisure-Time Exercise Questionnaire
HDL-C	High-density lipoprotein cholesterol
HOMA-IR	Homeostatic Model Assessment for Insulin Resistance
IL-6	Interleukin-6
LDL-C	Low-density lipoprotein cholesterol
MetS	Metabolic syndrome
PPO	Peak power output
RHR	Resting heart rate
SBP	Systolic blood pressure
SST	Serum separator tube
TNF-α	Tumor necrosis factor-alpha
VAT	Visceral adipose tissue
VO$_{2peak}$	Peak oxygen consumption
WC	Waist Circumference

INTRODUCTION

Tertiary academia is a predominantly desk-based workplace, wherein over 66% of academics report low-moderate levels of physical activity (Cooper & Barton, 2016). Low levels of physical activity can increase risk-factors associated with cardiometabolic disease, such as increased fat mass, chronic systemic inflammation and insulin resistance, whilst reducing protective factors such as lean mass and aerobic capacity (Hamer et al., 2012; Tsenkova, 2017). Furthermore, there appears to be underlying associations between risk factors, whereby markers of chronic systemic inflammation such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) have been associated with increased insulin resistance and fat mass, and decreased muscle mass (Hivert et al., 2008; Park, Park, & Yu, 2005). Accordingly, increasing physical activity in inactive academics may decrease the risk of metabolic syndrome (MetS) and the onset of cardiometabolic disease (Zhang et al., 2017).

Many workplaces assist employees to counter inactive lifestyles via exercise interventions to increase moderate to vigorous physical activity and improve aerobic capacity, body composition and components of MetS (de Sevilla, Vicente-Arche, Thuissard, Barcelo, & Perez-Ruiz, 2021). Onsite exercise interventions may be particularly effective within the academic workplace, where the engagement in moderate to vigorous physical activity is minimal (Safi, Cole, Kelly, & Walker, 2021), and long work hours may limit the leisure-time available for exercise (Fetherston, Fetherston, Batt, Sully, & Wei, 2020). However, despite the health consequences of low physical activity, the effectiveness of exercise training programs within tertiary academic populations remains to be fully explored.

Workplace exercise interventions can consist of combined endurance and resistance exercises (Concurrent training; CT), and CT increases aerobic capacity and muscle strength, whilst decreasing insulin resistance, body fat, total cholesterol and triglycerides within previously inactive adults (Brunelli et al., 2015; Donges et al., 2013; Libardi, De Souza, Cavaglieri, Madruga, & Chacon-Mikahil, 2012). However, there are conflicting results on the impact of CT on systemic inflammation in healthy adults (Donges et al., 2013; Ihalainen et al., 2018; Libardi et al., 2012), warranting further investigation into the association between changes in IL-6 and TNF-α, and alterations in other indicators of cardiometabolic health. CT increased peak oxygen consumption (VO$_{2peak}$) and strength, and decreased fat mass in University staff (e.g. academics, technical and professional staff) (Hunter, Gordon, Bird, & Benson, 2020), but the protective effects CT within the academic workplace remain to be explored in more detail.

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The primary aim of this study is to determine the effect of a 14-week concurrent exercise training program on components of MetS, insulin resistance, body composition and markers of systemic inflammation in inactive full-time academics. A secondary aim is to investigate associations between changes in systemic inflammation (IL-6, TNF-α) with changes in insulin resistance and body composition. We hypothesise that body composition, insulin resistance, systemic inflammation and components of MetS will improve with CT compared to control. Furthermore, positive associations are expected between changes in inflammatory cytokines with changes in body composition and insulin resistance.

METHODS

Participants and study design

This study is a 14-week randomised control trial. Participants (n=59) were stratified by age, sex and VO$_{2peak}$ and matched to the nearest neighbour. Matched participants were randomised in parallel groups of CT (n=29), or non-exercise control (n=30) at a 1:1 ratio. An independent third party generated a series of numbers via a computerized random number generator and another third party allocated matched participant codes according to the random number sequence (Urbaniak & Plous, 2019). The study was approved by a Human Research Ethics Committee (HREC REF: ETH18-3093) and registered with the Australian New Zealand Clinical Trials Registry (ACTRN12619000608167). CONSORT and CERT checklists are provided as online Appendices. Recruitment and testing commenced in June 2019 and was completed in December 2019. Schematic diagram of recruitment, retention and follow-up is shown in Figure 1. Participants from an Australian metropolitan university were recruited via local advertising and email to all academic staff. Potential participants attended a familiarisation session to provide verbal and written informed consent prior to completing a health pre-screening questionnaire (Exercise and Sport Science Australia adult pre-exercise screening tool). Inclusion criteria included 1) Physically inactive (Active Australia criteria; verbal and questionnaire-based assessment of <150 min/week of weighted physical activity); 2) aged between 35 and 65 years; and 3) working a minimum of 35 h per week at the university as an academic. Exclusion criteria included 1) pregnancy; 2) previous diagnoses of metabolic disease or musculoskeletal disorders; 3) pharmacological treatment for depression, diabetes, cardiovascular disease or inflammation; and 4) contraindications to exercise as identified in the health pre-screening.

Overview

Participants undertook a 60 min testing session for cardiometabolic health parameters and a 2-week period of data collection on lifestyle related variables before (July and August 2019) and after (November 2019) the 14-week intervention. Testing was conducted in a climate-controlled exercise physiology laboratory and outside of the primary teaching session. All assessors who measured key outcomes were blinded to group allocation. Participants arrived in a fasted state (10-12 h) at the testing facility between 6:00 and 9:00 am. Participants were required to avoid consumption of alcohol and refrain from exercise in the previous 24 h, wear basic exercise attire, void their bladder, and remove jewellery and metal objects. Participants then performed a series of tests, including 1) self-reported physical activity, blood pressure and resting heart rate (RHR); 2) body composition

via a Dual Energy X-ray Absorptiometry (DEXA) scan and anthropometry; 3) fasting venous blood sample collection, and; 4) aerobic capacity measured via a graded exercise test. Further, sociodemographic variables (research discipline, academic level, work hours, age, sex) were completed by participants on their smartphones or electronic devices using a downloaded software application (MetricWire Inc., 2019).

Procedures

Leisure-time Physical Activity

Leisure-time physical activity (including the CT sessions) was measured using the Godin Leisure-Time Exercise Questionnaire (GLTEQ), which is reported to have appropriate validity and reliability (Godin & Shephard, 1997). The GLTEQ includes 3-items used to measure the frequency of mild, moderate, and strenuous exercise during a normal 7-day period. Each exercise intensity is weighted and multiplied by how often it is performed and then scores are summed to provide a total weekly leisure activity score.

Blood Pressure and Resting Heart Rate

Participants rested in isolation in a seated position for at least 10 min. An automated blood pressure device (Omron 907, Omron Healthcare, Australia) then measured the respective means of RHR, systolic blood pressure (SBP) and diastolic blood pressure (DBP) from 3 separate measures recorded at 1-min intervals (SPRINT Research Group et al., 2015). Participants remained blind to the measurement results, thereby minimising any acute stress responses to the measure.

Anthropometry and Dual Energy X-ray Absorptiometry

Height was recorded using a stadiometer (Seca Asia-Pacific, Kuala Lumpur, Malaysia) and body mass was measured using a calibrated electronic scale (A&D Weighing, Sydney, Australia) in minimal clothing and without footwear. The resulting measurements were used to calculate body mass index (BMI). Waist Circumference (WC) was measured from the top of the iliac crest, at the end of normal expiration (NHLBI Obesity Education Initiative, 2000), and repeated twice. If the difference between the two measurements was greater than 1 cm, the two measurements were repeated and the mean calculated.

Participants underwent a whole-body DEXA scan in the supine position (Lunar Prodigy, GE Healthcare, Madison, WI, USA) (Shiel et al., 2017). The DEXA scan is a valid and reliable measure (Norcross & Van Loan,

2004), and was used to report absolute (kg) and relative (%) total body fat mass, android and gynoid fat mass and absolute (kg) total-body lean mass. Standardized body landmarks were used for reference and scans were analysed using enCORE software version 16 (GE Healthcare, Milwaukee, USA). Specifically, the android region of interest was set to 20% of the distance from the iliac crest to the base of the skull. Visceral adipose tissue (VAT) volume (cm^3) was estimated by manufacturer software as previously described (Olarescu et al., 2014). DEXA calibration was performed before each testing round according to the manufacturer's guidelines. Scanning mode was set to manufacturer defaults based on participant size, at a resolution of 4.8 x 13 mm.

Venous Blood Collection

Approximately 16 mL of fasting venous blood was collected in a serum separator tube (SST) and ethylenediaminetetraacetic acid (EDTA) tube. EDTA tubes were immediately centrifuged at 1300 g for 10 min at 18 °C whilst SST tubes clotted for 30 min before being centrifuged in the same manner. Serum and plasma were immediately stored at -80°C until analysis. Serum was used to measure lipid profile, including total cholesterol, high-density lipoprotein cholesterol (HDL-C), Non-HDL-C, low-density lipoprotein cholesterol (LDL-C) and triglycerides via the enzymatic colour test (Beckman Coulter AU5800; Beckman Coulter Inc., Brea CA, USA). Cholesterol hazard ratio was calculated as the total cholesterol divided by HDL-C. Glucose was measured using the hexokinase method (Beckman Coulter AU5800; Beckman Coulter Inc., Brea CA, USA). Plasma concentrations of IL-6, TNF-α and insulin were measured with chemiluminescent immunoassay (Magpix, Luminex Corporation, Texas, USA). For quality assurance, samples used for insulin, IL-6 and TNF-α measurement were analysed in duplicate with the derived mean used as the index value. Quality controls 1 and 2 were within the range of manufacturer recommendations. Insulin resistance was assessed via the Homeostatic Model Assessment (HOMA-IR) model-1(Matthews et al., 1985).

Aerobic Capacity

Aerobic capacity was assessed via the measurement of VO_{2peak} during a graded exercise test on a mechanically-braked cycle ergometer (Watt-bike Pro, Nottingham, United Kingdom). Participants commenced the test at 25 watts (W) and increased power output by 25 W each minute until volitional exhaustion. The average power output (W) was recorded at the completion of each 25W increment to determine peak power output (PPO). The mean of the highest three consecutive periods (10 s) of oxygen consumption was used to determine VO_{2peak}. Oxygen consumption was determined by measuring O_2 and CO_2 concentrations with a metabolic gas analyser

(Medgraphics Ultima System, Saint Paul, USA). The metabolic cart was calibrated according to the manufacturer's instructions, involving a pneumotachometer calibration via a 3 L syringe, analysis of ambient air, and gas calibration with a gravimetric gas mixture of known concentrations [CO_2 5.0 (0.02)%; O_2 12.0 (0.02)%].

Metabolic Syndrome classification

Metabolic syndrome was defined according to the criteria from Alberti et al. 2009 (Alberti et al., 2009). MetS was defined if participants present with 3 or more of the following 5 elements: 1) elevated WC (male $\geq$ 94 cm, female $\geq$ 80 cm); 2) elevated triglycerides ($\geq$ 1.7 mmol/L); 3) reduced HDL-C (HDL-C; < 1.0 mmol/L in males; < 1.3 mmol/L in females); 4) elevated blood pressure (systolic $\geq$ 130 and/or diastolic $\geq$ 85 mm Hg) or 5) elevated fasting glucose ($\geq$5.6 mmol/L).

Training and control conditions

The CT group trained for 60 min, three times per week for 14-weeks, with options of training before (6-9 am), during (11-1 pm) and after (4-7 pm) working hours. Training was conducted in small groups (2-6 participants) within a private climate-controlled exercise facility at the University campus and was performed under supervision by an accredited exercise scientist and trained third year undergraduate sport and exercise science students. The control group were instructed to maintain their normal lifestyle as determined using the GLTEQ.

The first week of training educated participants on the correct technique when completing exercises and familiarised participants with the equipment (machines, dumbbells, ergometers, benches). Table 1 shows the concurrent exercise training program including resistance and aerobic portions. Resistance training load was increased once a participant could complete the required number of repetitions with correct technique on all sets over two consecutive training sessions. Rest periods and repetition velocity were self-determined with consultation from training instructors. Participants were provided general encouragement to complete goal repetitions, and positive feedback when performing exercises with good technique. Training data (resistance training; sets, repetitions, weight. Endurance training; time, distance, power) were recorded in a customised training diary to monitor progressive overload. All training sessions started with a 5-7 min warm-up involving 3 min of low to moderate intensity aerobic exercise on rower and cycle ergometers, and resistance exercises at 50% working weight. After each session, static stretching of the primary muscle groups (15 s per muscle group) was undertaken. Importantly, resistance exercise was completed prior to endurance exercise to minimise any

potential interference effects (Coffey & Hawley, 2016). Any adverse events that occurred during exercise were recorded and stored in an online incident reporting system, though no adverse events were observed.

Statistical analysis

A per-protocol analysis was performed, whereby participants were excluded if their exercise adherence was more than 1SD below the mean (<55%). All normally distributed data are reported as mean ± standard deviation (SD) and skewed data are reported as median (interquartile range, IQR; difference between the third and first quartile). Normality and equal variance of data was assessed using the Shapiro-Wilk and Levenes test, respectively. Non-parametric analysis was completed on skewed variables (insulin, HOMA-IR, IL-6, TNF-α, android fat mass, VAT, total weekly leisure activity, SBP, and RHR) and parametric analysis was completed on log transformed (PPO, DBP, BMI, total fat mass (kg), total lean mass (kg), triglycerides, Non HDL-C and LDL-C) and all remaining normally distributed variables. Parametric analysis included a 2-way (time * group) repeated measures analysis of variance (ANOVA). If a significant time * group interaction effect was identified, paired t-tests were performed to determine within-group changes. Non-parametric analysis included a Mann-Whitney U test to assess between-group differences in change data, and the Wilcoxon signed-rank test analysed within-group differences. Effect sizes were determined using partial eta square (η_p^2) for parametric analysis (0.01 = small; 0.06 = moderate; 0.14 = large), and a standardised effect size for nonparametric analysis using $Z/\sqrt{N}$ (0.1 = small; 0.3 = moderate; 0.5 = large).

For the secondary aim, quantile regressions were used due to the non-normal distribution of the residuals in an OLS linear regression model. Quantile regressions at the median (q 0.5) were used to identify associations between body composition and insulin resistance as independent variables, and markers of systemic inflammation as dependent variables. Model 1 was adjusted for age, sex, height, group and independent variable * group interaction. Model 2 was further adjusted for fat mass (kg). Regression models were further conducted within each intervention group when there was a significant group interaction effect. Data are presented as a coefficient with 95% confidence interval (95% CI) with significance was accepted at $p<0.05$. Analyses were performed using SPSS Software, version 26 (IBM Corporation, Armonk, NY) and missing data were treated as missing in analyses. A priori sample size calculation was based on the smallest effect size of interest and performed using G*Power software (Version 3.1.9.3)(Faul, Erdfelder, Lang, & Buchner, 2007). A small effect of a 24-week CT intervention

on TNF-α in apparently healthy adults has been previously shown (Ihalainen et al., 2018). Therefore, 45 participants per group were required to detect effect size f of 0.15, alpha error of 0.05, and a power of 0.80. However, given resource constraints (limited gym and instructor availability) and a finite recruitment period (the intervention needed to be completed within the academic teaching period), 59 participants were recruited.

RESULTS

Participant and Training Characteristics

Baseline characteristics were similar for CT and control groups (Table 2). CT participants (n=28) completed a mean of 32 ± 10 of the 40 training sessions ($79 \pm 24\%$), and 3 participants were excluded from analyses due to non-adherence. CT participants included in analysis (n=23) completed a mean of 35 ± 5 sessions ($89 \pm 13\%$). There was a significant interaction effect for total weekly leisure activity (P=0.024, Z/√N=-0.326), showing an increase in CT (P<0.001) and no change in control (P=0.096).

Metabolic Syndrome, Insulin Resistance and Systemic Inflammation

There were 5 participants with MetS in CT (22%) and control (19%) at baseline, and 3 in CT (13%) and 6 in control (22%) following the intervention. Overall, there was a significant interaction effect for non-HDL-C (P=0.013, η_p^2=0.138), C:HDL (P=0.013, η_p^2=0.139) and glucose (P=0.047, η_p^2=0.091). However, post-hoc analysis reported no within-group changes for non-HDL-C (CT P=0.099; control P=0.067), C:HDL (CT P=0.094; control P=0.071), and glucose (CT P=0.120; control P=0.157). There was a significant interaction effect for WC (P=0.002, η_p^2=0.184), which showed an increase in control (P=0.001) and no change in CT (P=0.474). No significant interaction effects were reported for HOMA-IR, insulin, IL-6, TNF-α, triglycerides, total cholesterol, HDL-C, LDL-C, DBP or SBP (Table 3, P>0.05).

Body Composition and Aerobic Fitness

Body composition and aerobic capacity results are shown in Table 4. In response to CT, there was an interaction effect for absolute (P=0.0l9, η_p^2=0.109) and relative total fat mass (P=0.001, η_p^2=0.218) with a decrease in CT (kg P=0.008, % P=<0.001) and no change in control (kg P=0.765, % P=0.937). A significant interaction effect was shown for android fat mass (kg; P=0.017, Z/√N=0.337; % P=0.032, η_p^2=0.093), whereby a within-group decrease in absolute android fat mass was found for CT (kg P=0.042, % P=0.075), without change in control (kg P=0.105, % P=0.229). There was an interaction effect for VAT (P=0.009, Z/√N=0.369) which decreased in CT

(P=0.021) and did not change in control (P=0.199). There was also an interaction effect for lean mass (P=0.002, η_p^2=0.185) which increased in CT (P<0.001) and did not change in control (P=0.413). There were no significant interaction effects for gynoid fat mass or BMI following the intervention (P>0.05).

An interaction effect was evident for RHR (P=0.042, Z/√N=0.294), with a decrease in CT (P=0.002) and no change in control (P=0.302). An interaction effect was also found for PPO (P<0.001, η_p^2=0.433) with an increase in CT (P<0.001) and no change in control (P=0.737). An interaction effect was evident for VO$_{2peak}$ (P<0.001, η_p^2=0.296), which increased in CT (P<0.001) and did not change in control (P=0.769).

Associations between Body Composition, Insulin Resistance and Systemic Inflammation

Regression models showed a significant group interaction effect for changes in HOMA-IR (P=0.006) and fasting insulin (P=0.006) in association with IL-6 (Table 5). Post-hoc analysis showed that changes in HOMA-IR and fasting insulin had a significant positive association with IL-6 in the control group (P<0.001) and this association remained following adjustment for changes in fat mass (P<0.001). No significant associations or group interaction effects (P>0.05) were evident between change in body composition variables and change in markers of systemic inflammation.

Discussion

Our findings support the use of CT to improve various cardiometabolic risk markers within inactive academic employees. Specifically, 14-weeks of CT decreased central adiposity and increased lean muscle mass and aerobic capacity. However, there were no changes in systemic inflammation or insulin resistance. Although there were no associations between changes in fat mass and changes in systemic inflammation, there was a positive association between changes in insulin resistance and changes in IL-6 in the control, but not the training group. Given the adherence (79%) to the intervention, our results indicate that an onsite CT program is an effective method to combat inactivity within the academic workplace and reduce some of the risk factors associated with the development of type 2 diabetes and cardiovascular disease.

To our knowledge, this is the first study to investigate the impact of CT on the cardiometabolic health of inactive academics. Despite the observed reduction in the number of participants with MetS in the CT group, the sample size was too small to statistically compare effects between groups. Furthermore, despite an interaction effect for components of MetS (ie. fasting glucose, non HDL-C and C:HDL), there were no significant within-group changes in these risk markers, likely due to the limited study power. Comparative data on exercise training in academics is minimal, but other CT interventions within inactive adults have not altered glucose or lipid profile (Langleite et al., 2016; Schroeder, Franke, Sharp, & Lee, 2019). HOMA-IR also remained unchanged in the current academic cohort, whilst other studies in adults without pre-existing diabetes have reported mixed results (Brunelli et al., 2015; Jamka et al., 2021). It is suggested that these outcomes may be influenced by exercise adherence, intensity and intervention duration, but the training variables that have the largest effect remain equivocal (Conn et al., 2014). Furthermore, given our participants had not been previously diagnosed with metabolic disease, there may have been a ceiling effect on improvements to metabolic blood markers (Lin et al., 2015). Regardless, the interaction effects we report in fasting glucose and the lipid profile prompt further research with larger samples into the impact of CT on these components of MetS in inactive academics.

Previous prospective research has reported that regular CT reduces the risk of developing MetS (Bakker et al., 2017). Our results highlight the potential of CT to protect against risk factors of MetS through a decrease in total and central adiposity. Other workplace studies have reported significant improvements in total body fat mass following CT (Hunter et al., 2020), but few have reported changes in regional body fat distribution. The decrease in central adiposity (VAT and android fat mass) is particularly important given its strong association

with proinflammatory cytokine activity and insulin resistance (Preis et al., 2010). Further, we found large increases in lean mass alongside increases in aerobic capacity, indicating concurrent adaptations to both endurance and resistance training (Coffey & Hawley, 2016). Though research within academics is limited, CT studies in other untrained populations have reported mixed results for a change in lean mass (Donges et al., 2013; Schroeder et al., 2019), which may be due to low statistical power given the small group sizes. Regardless, BMI did not change as a likely result of contrasting changes in fat mass and lean mass, emphasising the primary limitation of BMI as not differentiating between these variables. The improvements to body composition are important for reducing the risk of MetS and type 2 diabetes, which have detrimental impacts on workplace productivity (Schultz & Edington, 2009). In turn, our findings may have important implications for the tertiary education sector given the vital teaching and research roles performed by academics in universities.

Systemic inflammation did not change in response to CT, which is similar to previous studies completed in inactive apparently healthy adults (Donges et al., 2013; Libardi et al., 2012). This lack of change may be due to participants being free of pre-existing cardiometabolic disease at baseline. Indeed, exercise decreases IL-6 in individuals with type 2 diabetes (Hayashino et al., 2014), but has mixed effects on IL-6 and no effect on TNF-α in apparently healthy inactive adults (Cronin, Keohane, Molloy, & Shanahan, 2017). Notwithstanding, previous findings show a positive relationship between fat mass and IL-6 and TNF-α (Park et al., 2005). Thus, regular CT may prevent inactive academics from low-grade chronic systemic inflammation and concomitant risk of metabolic disease through modulation of fat mass (Spranger et al., 2003).

There were no relationships between changes in body composition and markers of systemic inflammation. This is surprising given that CT decreased fat mass and VAT, which are primary sources of IL-6 and TNF-α production (Fain, Madan, Hiler, Cheema, & Bahouth, 2004; Villarroya, Cereijo, Gavalda-Navarro, Villarroya, & Giralt, 2018). Regardless, other CT research has also reported decreases in measures of fat mass without concomitant decreases in IL-6 and TNF-α (Ihalainen et al., 2018; Langleite et al., 2016). However, prospective studies have found that measures of fat mass at least partially account for the positive association between IL-6 and TNF-α and metabolic disease (Spranger et al., 2003), though few have investigated the association between changes in fat mass and changes in systemic inflammation. It is also likely that changes in other variables such as adipose tissue macrophage phenotype, adipose tissue type, and insulin resistance are associated with changes in IL-6 and TNF-α (Hotamisligil, 2017). Indeed, we found that changes in fasting insulin and HOMA-IR were

positively associated with IL-6 in the control group, which was independent of fat mass. Whilst this independent relationship has been found in other populations (Kern, Ranganathan, Li, Wood, & Ranganathan, 2001), it was not evident in our CT group, indicating that CT may attenuate the association between insulin resistance and IL-6. Indeed, IL-6 is a complex cytokine with various effects dependent on the location of its release and mode of action, which can be influenced by exercise (Pedersen, 2011). Although we did not investigate the reasons for the lack of association in CT, our findings prompt further investigation into how exercise can influence the association between insulin resistance and IL-6.

Limitations

This study shows the benefits of CT for apparently healthy inactive academics but limits the generalisability of our findings to other inactive workplaces and the wider academic population. Indeed, exercise has a greater impact on systemic inflammation, insulin resistance and other metabolic blood markers in individuals with pre-existing metabolic conditions, which may also clarify associations between changes in these variables. Furthermore, our sample size was underpowered to detect changes in inflammatory markers, though they were the smallest effect sizes of interest. These limitations could be overcome in the future by using a larger multicentre longitudinal design and investigating the impact of CT on academics with and without metabolic disease.

Conclusions

This study reports that a 14-week (onsite) CT program with 79% adherence is effective in improving fat mass, fat distribution, lean mass and aerobic capacity in inactive academics. However, there were no changes to insulin resistance or systemic inflammation in this apparently healthy cohort. The study prompts further research into the relationship between insulin resistance and IL-6 given the positive association evident in the control group, but not CT. Overall, this study conveys the effectiveness of combined endurance and resistance training in reducing risk factors associated with low levels of physical activity in the academic workplace.

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Table 1

Concurrent Training Program.

	Week 1	Week 2	Week 3	Weeks 4 to 7	Weeks 8 to 14	Variables used to monitor progressive overload
Resistance exercises	2 sessions x 1 set x 8-12 reps: Leg press Split squat Seated hamstring curl Chest press Lat pulldown	2 sessions x 2 sets x 8-12 reps: Leg press Split squat Seated hamstring curl Chest press Lat pulldown	3 sessions x 2 sets x 8-12 reps: Leg press Split squat Seated hamstring curl Chest press Lat pulldown	3 sessions x 3 sets x 8-12 reps: Leg press Split squat Seated hamstring curl Chest press Lat pulldown	3 sessions x 3 sets x 8-12 reps: Leg press Split squat Hip thrust Chest press Cable row	Training volume = session frequency x sets x reps x weight (kg)
Resistance Exercise Volume *	1748 ± 791	4638 ± 2242	8334 ± 4179	Week 4; 15186 ± 7141 Week 7; 20447 ± 8154	Week 8; 14855 ± 7948 Week 14; $9208 \pm 10039^{\#}$	
Resistance Exercise Weight (kg) *†	15 ± 7	19 ± 9	23 ± 11	Week 4; 28 ± 14 Week 7; 39 ± 15	Week 8; 28 ± 15 Week 14; 39 ± 11	
Endurance exercise	7.5 min each: Row ergometer Cycle ergometer	7.5min each: Row ergometer Cycle ergometer	7.5min each: Row ergometer Cycle ergometer	8 to 9min each: Row ergometer Cycle ergometer	9 to 11min each: Row ergometer Cycle ergometer	Duration, distance (km) and average power output (W)
Row Distance (km) *	2514 ± 522	2817 ± 474	4387 ± 660	Week 4; 4698 ± 741 Week 7; 5390 ± 729	Week 8; 5403 ± 741 Week 14; 4814 ± 1587	
Row Power (W) *	67 ± 42	90 ± 46	99 ± 45	Week 4; 106 ± 44 Week 7; 110 ± 42	Week 8; 115 ± 42 Week 14; 116 ± 33	
Bike Distance (km) *	5.7 ± 0.9	6.2 ± 0.9	9.3 ± 1.2	Week 4; 11.4 ± 6.4 Week 7; 11.0 ± 1.4	Week 8; 10.7 ± 1.5 Week 14; 8.8 ± 2.6	

All data reported as mean ± SD.

[#] *Exercise adherence was monitored sequentially, and thus sessions missed in the earlier weeks of training were evidenced in week 14, resulting in lower training volume in week 14 compared to week 8*

[*] Week 7 significantly higher than week 1 ($p<0.001$)

[†] Week 14 significantly higher than week 8 ($p<0.05$)

Table 2

Baseline Characteristics of Participants in Intervention and Control Groups

Characteristics	Intervention (n=23)	Control (n=27)
Age (years), mean ± SD	49 ± 9	50 ± 8
Female Sex, n (%)	16 (70)	18 (66)
VO_{2peak}, mean ± SD	28.9 ± 5.7	29.5 ± 6.1
Leisure-Time Physical Activity Score, median (IQR)*	17 (27)	21 (22)
Body Mass Index (kg/m^2), n (%)		
Underweight (<18.5)	1 (4)	1 (4)
Normal (18.5-24.9)	13 (57)	12 (44)
Overweight (25.0-29.9)	7 (30)	9 (33)
Obese (≥30)	2 (9)	5 (19)
Academic Discipline, n (%)		
HASS	13 (56)	16 (59)
STEM	10 (44)	11 (41)
Academic Level, n (%)		
Associate Lecturer	1 (4)	1 (4)
Lecturer	9 (39)	12 (44)
Senior Lecturer	8 (35)	7 (26)
Associate Professor (Reader)	1 (4)	2 (7)
Professor	4 (17)	5 (19)
Daily Work Hours, median (IQR)	8.8 (1.2)	8.7 (2.1)

Abbreviation: VO_{2Peak}, peak volume of oxygen consumed during graded exercise test; HASS; Humanities, Arts, and Social Sciences; STEM, Science, Technology, Engineering, and Mathematics.

* Measured using the GLTEQ

Table 3

Components of the Metabolic Syndrome, Systemic Inflammation and Insulin Resistance Before and After the Intervention

Variables		Concurrent Training				Control			Time by Group
	n	Pre	Post	Change	n	Pre	Post	Change	P value (Effect Size)
MetS, n (%)	23	5 (22)	3 (13)	-2 (9)	27	5 (19)	6 (22)	1 (4)	
SBP (mmHg)	23	121 (15)	114 (14)	-3 (9)	27	117 (16)	113 (22)	-4 (8)	0.891 (-0.019)
DBP (mmHg)	23	74 (10)	70 (14)	-3 (7)	27	70 (17)	72 (12)	-1 (6)	0.155 (0.042)
WC (cm)	23	92.7 ± 9.9	92.3 ± 10.2	-0.3 ± 2.2	27	93.8 ± 12.2	95.7 ± 12.3†	1.8 ± 2.4	**0.002 (0.184)**
Glucose (mmol/L)	19	5.27 ± 0.46	5.17 ± 0.37	-0.10 ± 0.27	25	5.13 ± 0.41	5.24 ± 0.40	0.12 ± 0.40	**0.047 (0.091)**
Triglycerides (mmol/L)	19	1.2 (0.6)	1.1 (0.5)	0.0 (0.4)	25	1.1 (0.6)	1.1 (0.9)	0.0 (0.6)	0.587 (0.007)
HDL-C (mmol/L)	19	1.53 ± 0.31	1.58 ± 0.38	0.05 ± 0.21	25	1.44 ± 0.32	1.44 ± 0.29	-0.01 ± 0.16	0.322 (0.023)
Total Cholesterol (mmol/L)	19	5.78 ± 0.78	5.64 ± 0.83	-0.14 ± 0.52	25	5.35 ± 1.15	5.49 ± 1.03	0.14 ± 0.48	0.070 (0.076)
Non-HDL-C (mmol/L)	19	4.1 (1.2)	4.1 (1.0)	-0.1 (0.6)	25	3.8 (2.0)	4.0 (1.8)	0.1 (0.5)	**0.013 (0.138)**
LDL-C (mmol/L)	19	3.5 (1.1)	3.4 (0.7)	-0.1 (0.6)	25	3.2 (1.5)	3.4 (1.5)	0.1 (0.5)	0.051 (0.088)
C:HDL (mmol/L)	19	3.90 ± 0.86	3.73 ± 0.92	-0.17 ± 0.43	25	3.81 ± 0.89	3.95 ± 1.01	0.14 ± 0.36	**0.013 (0.139)**
Insulin (uIU/ml)	18	5.18 (6.31)	4.05 (6.57)	-0.95 (1.92)	25	5.29 (10.42)	5.20 (14.02)	-0.28 (3.11)	0.375 (0.135)
HOMA-IR	18	1.29 (1.69)	0.95 (1.61)	-0.23 (0.56)	25	1.20 (2.39)	1.15 (3.34)	0.00 (0.85)	0.115 (0.240)
IL-6 (pg/ml)	15	0.77 (14.24)	1.28 (14.27)	0.05 (1.37)	22	5.30 (16.54)	4.82 (24.35)	-0.30 (4.93)	0.143 (-0.244)
TNF-α (pg/ml)	18	1.57 (1.31)	1.74 (1.55)	0.02 (0.29)	25	1.93 (1.04)	1.67 (0.93)	-0.04 (0.58)	0.796 (-0.039)

Data are reported as median (IQR) or mean ± SD. Abbreviations: MetS, metabolic syndrome; SBP, systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; C:HDL, cholesterol hazard ratio; HOMA-IR, homeostatic model assessment of insulin resistance; IL-6, Interleukin-6; TNF-α, tumor necrosis factor-alpha.

† Significant change in response to the intervention (P<0.05)

Table 4

Body Composition, Aerobic Capacity and Physical Activity Results Before and After the Intervention

Variables	Concurrent Training				Control				Time by Group
	n	Pre	Post	Change	n	Pre	Post	Change	P value (Effect Size)
BMI (kg/m^2)	23	24.36 (3.46)	24.72 (3.45)	0.12 (0.69)	27	26.08 (5.24)	25.57 (5.79)	0.12 (0.80)	0.874 (0.001)
Height (cm)	23	170.73 ± 8.46	170.75 ± 8.53	0.02 ± 0.74	27	170.60 ± 7.40	170.39 ± 7.32	-0.21 ± 0.63	0.241 (0.028)
Weight (kg)	23	73.09 ± 14.68	73.56 ± 14.80	0.46 ± 1.44	27	74.94 ± 14.71	75.19 ± 14.35	0.25 ± 1.77	0.646 (0.004)
Total Fat Mass (kg)	23	24.00 (8.35)	22.53 (9.14)†	-0.63 (1.27)	27	25.70 (14.74)	26.01 (14.83)	0.18 (1.25)	**0.019 (0.109)**
Total Lean Mass (kg)	23	41.38 (11.00)	42.86 (12.41)†	1.35 (1.86)	27	44.28 (8.17)	44.63 (8.05)	0.17 (1.81)	**0.002 (0.185)**
Total fat mass (%)	23	34.3 ± 7.6	33.0 ± 8.1†	-1.3 ± 1.4	27	34.4 ± 9.1	34.4 ± 9.3	0.0 ± 1.1	**0.001 (0.218)**
Android (kg)	23	1.97 (0.69)	1.80 (0.92)†	-0.06 (0.27)	27	2.14 (1.38)	1.93 (1.44)	0.04 (0.17)	**0.017 (0.337)**
Android (%)	23	7.7 ± 1.8	7.5 ± 1.8	-0.2 ± 0.4	27	8.2 ± 1.9	8.3 ± 1.9	-0.1 ± 0.4	**0.032 (0.093)**
Gynoid (kg)	23	4.58 ± 1.59	4.49 ± 1.63	-0.10 ± 0.27	27	4.68 ± 2.24	4.65 ± 2.15	-0.03 ± 0.27	0.36 (0.017)
Gynoid (%)	23	18.3 ± 3.3	18.4 ± 3.4	0.1 ± 0.5	27	17.4 ± 2.8	17.4 ± 2.7	0.0 ± 0.6	0.367 (0.017)
VAT volume (cm^3)	23	663 (685)	553 (715)†	-66 (110)	27	779 (761)	759 (1093)	37 (167)	**0.009 (0.369)**
VO$_{2peak}$ (mL/kg/min)	22	28.9 ± 5.7	32.9 ± 6.9†	4.0 ± 3.1	25	29.5 ± 6.1	29.3 ± 5.6	-0.2 ± 3.4	**<0.001 (0.296)**
PPO (watts)	23	151 (72)	174 (97)†	22 (31)	25	153 (49)	154 (54)	-1 (8)	**<0.001 (0.433)**
RHR (bpm)	23	69 (10)	64 (12)†	-5 (9)	25	67 (9)	65 (12)	0 (10)	**0.042 (0.294)**
Total weekly leisure activity	22	17 (27)	41 (20)†	21(19)	26	21 (22)	24 (40)	4 (28)	**0.024 (0.326)**

Data are reported as median (IQR) or mean ± SD. Abbreviations: BMI, body mass index; VAT, visceral adipose tissue; VO$_{2Peak}$, peak volume of oxygen consumed during graded exercise test; PPO, peak power output; RHR, resting heart rate.

† Significant change in response to the intervention (P<0.05)

Table 5

Associations Between Changes in Insulin Resistance and Body Composition and Changes in Systemic Inflammation.

	Dependent Variables							
	Model 1				**Model 2**			
	Δ IL-6 (pg/ml)	**P**	**Δ TNF-α** (pg/ml)	**P**	**Δ IL-6** (pg/ml)	**P**	**Δ TNF-α** (pg/ml)	**P**
Δ Fat Mass (kg)	0.997 (-4.045, 6.038)	0.689	-0.283 (-0.727, 0.161)	0.204	-	-	-	-
Δ Lean mass (kg)	0.097 (-0.229, 0.423)	0.549	0.340 (-5.167, 5.846)	0.901	0.652 (-5.658, 6.962)	0.834	0.167 (-0.183, 0.517)	0.340
Δ Android Mass (kg)	2.165 (-28.597, 32.927)	0.887	-1.637 (-4.302, 1.027)	0.221	1.953 (-26.927, 30.832)	0.891	-3.433 (-6.922, 0.056)	0.054
Δ Gynoid Mass (kg)	3.237 (-20.226, 26.699)	0.780	-0.727 (-2.867, 1.412)	0.495	1.169 (-18.547, 20.884)	0.904	-1.543 (-3.790, 0.705)	0.172
Δ VAT Volume (cm^3)	-0.004 (-0.051, 0.043)	0.863	-0.002 (-0.005, 0.002)	0.345	0.003 (-0.040, 0.045)	0.898	-0.001 (-0.006, 0.003)	0.620
Δ HOMA-IR	-7.957 (-17.157, 1.243)	0.088[†]	0.085 (-0.653, 0.822)	0.817	-4.955 (-13.173, 3.264)	0.227[†]	0.304 (-0.632, 1.239)	0.515
Intervention	-0.650 (-7.521, 6.222)	0.837	-	-	-0.114 (-8.373, 8.145)	0.976	-	-
Control	6.604 (4.150, 9.058)	<0.001	-	-	5.957 (2.961, 8.953)	<0.001	-	-
Δ Fasting Glucose	-0.763 (-22.644, 21.119)	0.944	0.418 (-0.956, 1.791)	0.541	1.618 (-14.404, 17.641)	0.838	1.052 (-0.192, 2.295)	0.095
Δ Fasting Insulin	-1.262 (-3.192, 0.667)	0.192[†]	-0.028 (-0.217, 0.162)	0.769	-1.090 (-2.955, 0.775)	0.242[†]	-0.024 (-0.219, 0.171)	0.804
Intervention	0.115 (-2.227, 2.457)	0.915	-	-	0.619 (-1.896, 3.134)	0.591	-	-
Control	1.926 (1.378, 2.473)	<0.001	-	-	1.787 (1.137, 2.437)	<0.001	-	-

Quantile regressions are reported as coefficients (95% confidence intervals, CI) at the median (q 0.5)

Model 1: adjusted for age, sex, height, group and group interaction

Model 2: adjusted for age, sex, height, fat mass (kg), group and group interaction.

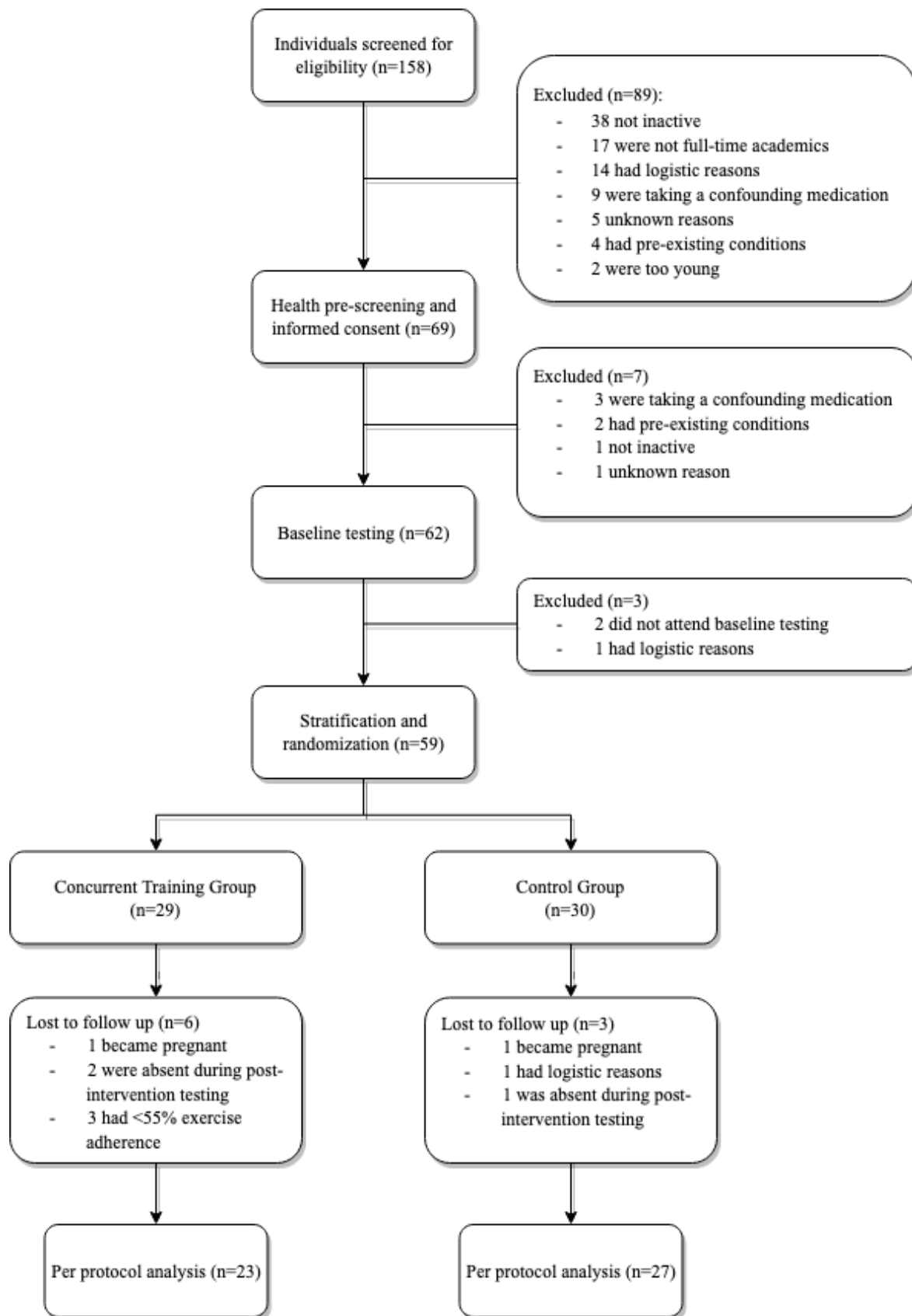[†] Interaction effect for group

Final sample n=43.

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) Flow Diagram