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ORIGINAL ARTICLE

Inflammatory, lipid, and body composition responses to interval training or moderate aerobic training

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Abstract
Purpose The goal of this study was to compare the effect of work- and duration-matched interval training (HIIT) versus moderate aerobic endurance training (ET) on acute and chronic inflammation, along with changes in the lipid profile, to determine which may be more beneficial for improving cardiovascular health.
Methods Twelve sedentary males (maximal oxygen consumption = 41.6 ± 5.4 mL kg^{-1} min^{-1}) completed 8 weeks of aerobic interval training or moderate aerobic training, with variables including C-reactive protein (CRP) for chronic inflammation, interleukin-6 (IL-6) response for the acute inflammatory response, plasma concentrations of high-density lipoprotein (HDL), total cholesterol (TC), triglycerides (TRG), and low-density lipoprotein, and body composition measured before and after the training period.
Results HIIT decreased plasma TRG from 92 ± 32 to 61 ± 12 mg dL^{-1}, which was significantly different from ET, while ET improved the TC:HDL ratio from 4.67 ± 0.85 to 4.07 ± 0.96 and reduced the percentage of android fat from 36.78 ± 9.60 to 34.18 ± 11.39 %. Neither training protocol resulted in an acute IL-6 response on the first nor the last day of exercise, a change in chronic levels of CRP, or a significant increase in HDL, despite previous research finding these changes.
Conclusions It seems that in order to maximize the health outcomes from physical activity, both HIIT and ET should be included. The acute inflammatory response and reductions in chronic inflammation resulting from exercise training may not be as common as the literature suggests.

Keywords Inflammation · Aerobic interval training · Body composition · Cholesterol · Heart disease

Abbreviations

ANOVA	Analysis of variance
CHD	Coronary heart disease
CRP	C-reactive protein
ET	Endurance training
Glu	Glucose
HDL	High-density lipoprotein
HIIT	High-intensity interval training
IL-6	Interleukin-6
LDL	Low-density lipoprotein
TC	Total cholesterol
TRG	Plasma triglyceride concentration
VO_{2max}	Maximal oxygen consumption per minute
$V_{VO_{2max}}$	Maximal aerobic running velocity

Introduction

High-density lipoprotein (HDL) plays a vital role in the prevention of atherosclerosis and coronary heart disease (CHD) (Gordon et al. 1977). While evidence suggests an inverse association between HDL concentrations and risk of CHD events (Ridker et al. 2000), individuals with

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normal to high (≥60 mg dL^{-1}) concentrations of HDL are not necessarily protected from CHD. For instance, in the Framingham Heart Study, 44 % of men and 43 % of women who had a CHD event had HDL concentrations above the recommended levels (Ansell et al. 2003).

The failure of HDL to protect against a CHD event can be at least partially explained by an altered functional ability of HDL. Ansell et al. (2003) compared the HDL function of seemingly healthy individuals to those diagnosed with CHD and found that even when concentrations were matched, HDL from CHD patients was more pro-inflammatory and less capable of reverse cholesterol transport. It is believed that the persistent low-grade inflammation associated with CHD is a cause of the reduced HDL function (Ansell et al. 2003).

In the acute inflammatory response to an endotoxemic challenge, the structure of HDL is modified, losing apolipoprotein A-1 subunits and gaining serum amyloid A subunits, resulting in a pro-inflammatory HDL molecule or an oxidized HDL molecule that enhances the formation of oxidized low-density lipoprotein (LDL) (VanLenten et al. 1995; Lindhorst et al. 1997). It is therefore not surprising that chronic inflammation matched with increased pro-inflammatory HDL and oxidized HDL is a strong predictor of CHD mortality, regardless of HDL concentration (Ansell et al. 2003). Resolution of an inflammatory state results in HDL regaining its anti-inflammatory properties (Lindhorst et al. 1997).

Regular exercise has the beneficial effect of reducing chronic inflammation (Aronson et al. 2004), which could explain how exercise also increases HDL concentration and HDL anti-inflammatory function, decreasing the risk of CHD (Mora et al. 2007). This adaptation is potentially the result of repeated, exercise-induced inflammatory challenges that result in greater anti-oxidant enzyme function (Hellsten et al. 1996). Therefore, exercise protocols that result in greater acute inflammatory responses could potentially result in greater reductions in chronic inflammation, and thus greater HDL concentrations and function. In this regard, Leggate et al. (2010) demonstrated that high-intensity interval training (HIIT) generates a greater acute inflammatory response in the form of elevated interleukin-6 (IL-6) than work-matched moderate intensity endurance training (ET), which is consistent with the finding that greater exercise intensities are associated with greater inflammatory challenges (Ostrowski et al. 2000). These findings provide a mechanism for previous research findings which show that HIIT may be more beneficial than ET for reducing chronic inflammation (Hellsten et al. 1996), and provide a potential mechanism by which HIIT could result in greater improvements in the lipid profile than ET.

Adaptations to HIIT and ET have been compared for a wide range of variables, with HIIT demonstrating equal or greater improvements in areas such as cardiovascular fitness and rehabilitation (Wisløff et al. 2007), body composition (Boutcher 2011), and metabolic health (Tjønna et al. 2008). However, the term HIIT encompasses a nearly infinite combination of work and recovery interval intensities and durations, and not all HIIT protocols generate the same degree of adaptive response (Stepto et al. 1999). Leggate et al. (2010) employed a protocol with a total time at high intensity (40 min total at ~88 % VO_{2peak}), and thus training stimulus, that was much greater than what is commonly employed (Wisløff et al. 2007; Burgomaster et al. 2008), and much longer than necessary to elevate acute IL-6 concentrations (Nielsen et al. 1996). Thus, it is not known whether HIIT protocols with shorter total work durations result in the same acute inflammatory response as seen by Leggate et al.

Therefore, the purpose of this study is to compare the effect of a HIIT protocol with a common total work interval duration versus work- and duration-matched ET on acute and chronic inflammatory responses and the blood lipid profile. We hypothesized that HIIT would result in greater adaptations of blood lipids and a greater reduction in chronic inflammatory markers than ET due to greater acute inflammatory challenges resulting from HIIT. Reductions in chronic inflammation would indicate an environment in which a greater number of HDL molecules would maintain an anti-inflammatory role.

Methods and procedures

Participants

Participants were recruited by word of mouth from the local community. A power analysis prior to participant recruitment indicated that at least five participants in each group were needed to detect similar changes in HDL concentration (Musa et al. 2009) and acute IL-6 response (Meckel et al. 2009) with HIIT as has previously been found, with a power of 0.80. Fourteen sedentary-to-inactive, but healthy, male volunteers (age 21.4 ± 1.6 years) were included in this study. Criteria for participation included not meeting the amount of weekly physical activity recommended by the American College of Sports Medicine (Whaley et al. 2006), and not using medications that could increase the risks associated with vigorous intensity physical activity or affect testing variables, such as antihypertensive, antihyperlipidemic, antiarrhythmic, anti-inflammatory, and corticosteroidal medications. No participants were dyslipidemic (total cholesterol >200 mg dL^{-1}) or hypertensive (blood pressure >140/90 mmHg) at the start of the study. Females were not included due to the variability in blood lipid profile during the menstrual cycle, which is exacerbated by

the use of oral contraceptives (Demacker et al. 1982; Cullinane et al. 1995). The study protocol was reviewed and approved by the Auburn University Institutional Review Board. Informed consent was obtained from all individual participants included in the study.

Study design

Participants were placed into matched groups based on HDL concentration and VO_{2max}: a HIIT group and a moderate ET group. There were no significant differences in baseline values between groups for any of the variables measured in this study. Table 1 provides general participant characteristics.

Each group completed a battery of tests before and after 8 weeks of training, with measurements including a complete lipid profile, chronic inflammation, body composition, and VO_{2max}. Chronic inflammation was determined by blood concentrations of C-reactive protein (CRP). On the first and final days of training, blood samples were collected before and after exercise in order to examine the acute inflammatory response, as determined by IL-6 concentrations in the blood. An additional VO_{2max} test was completed after 4 weeks of training in order to update the training protocols in an effort to prevent potential plateaus in adaptation (Hickson et al. 1981).

One participant in the ET group withdrew from the study due to an ankle injury unrelated to activities involved in the study. In order to maintain closely matched groups, data from the participant with the most similar baseline values in the HIIT group was not analyzed or included in the results. Thus, 12 participants completed the study and were included in the data analysis.

Testing days

Participants were asked to refrain from vigorous activity for 2 days prior to reporting to the lab for the initial testing day, and were given 72–96 h of rest between the final training day and the post-testing session to negate any inflammatory response from previous activity. Participants were also instructed to refrain from consuming alcohol and caffeine for 24 h before the testing day, and to come to the lab after an overnight fast, allowing the inflammatory response to feeding to subside and the lipid profile to be measured at a fasting level. Height was determined with a stadiometer and weight (Michelli Scales, Harahan, LA) was recorded to the nearest 0.25 kg. Body composition was determined using dual X-ray absorbance (GE Healthcare Lunar, Madison, WI). Blood pressure was measured using a sphygmomanometer after sitting quietly for 10 min in a semi-reclined position to ensure that none of the participants were hypertensive. The blood lipid profile was then determined via whole blood sample acquired by finger prick using the Cholestech LDX system (Alere Inc., Waltham, MA). Another blood sample was then collected via venipuncture to measure CRP. Finally, participants completed an incremental exercise test to determine VO_{2max} and the speed that elicits VO_{2max} ($V_{VO_{2max}}$).

Table 1 Participant characteristics

	HIIT	ET	*p* value
Age (years)	21.4 ± 1.1	21.8 ± 2.1	0.66
Height (m)	1.80 ± 0.05	1.83 ± 2.1	0.66
Weight (kg)	81.9 ± 10.0	90.2 ± 21.1	0.40
Body fat (%)	28.23 ± 7.03	27.90 ± 7.97	0.94
BMI (kg m^{-2})	24.7 ± 2.9	27.1 ± 4.8	0.33
VO_{2max} (mL kg^{-1} min^{-1})	41.4 ± 5.5	41.9 ± 5.8	0.87

All values are presented as mean ± SD

Blood sample collection

Blood samples were collected via finger prick (for blood lipid analysis) and venipuncture using aseptic technique by a trained phlebotomist. Samples to be used for determining chronic inflammation and acute inflammatory response were collected in sodium heparin-treated tubes (Vacutainer, Becton Dickenson, Franklin Lakes, NJ). Sodium heparin treated samples were centrifuged within 10 min of sample collection for 10 min at 6000 rpm and 0 °C. The plasma was then transferred into 1.5 mL microtubes and stored for later analysis at −80 °C.

Chronic inflammation

CRP was determined before the start of training and at the end of the 8-week training period using a human CRP sandwich enzyme immunoassay (Quantikine ELISA, R&D Systems, Minneapolis, MN). Plasma samples were diluted 100-fold with calibrator diluent, with 50 µL of sample added to each well. After addition of CRP conjugate and incubation, substrate solution was added to each well and allowed to incubate for 30 min. Stop solution was then added and absorbance was read at 570 and 450 nm; wavelength subtraction [optical density (OD) at 570 nm–OD 450 nm] was applied to analyze data. All samples were measured in triplicate, and the intra-assay coefficient of variation for this assay was 6.63 %.

Acute inflammatory response

The acute inflammatory response to the different exercise protocols and the change in acute inflammatory response after 8 weeks of exercise were determined by measuring

plasma IL-6 concentrations from samples drawn immediately before and within 2 min after the exercise sessions on the first and last day of exercise in the study. Plasma IL-6 concentrations were measured using a human IL-6 enzyme immunoassay (ELISA Ready-Set-Go!, eBioscience, San Diego, CA). Plates were coated with capture antibody in coating buffer and blocked with assay diluent. 100 µL of plasma was added to each well followed by an overnight incubation. Detection antibody, substrate solution, and, after a 30 min incubation, stop solution were added. Absorbance was read at 450 and 570 nm for wavelength subtraction. All samples were measured in triplicate, with a high-low inter-assay coefficient of variation of 0.04–9.71 % and intra-assay coefficients of variation of 8.70 and 9.78 %.

Blood lipid profile

A complete blood lipid profile was acquired using the Cholestech LDX system with Lipid Profile + Glu cartridges. The whole blood sample was analyzed within 20 s after initial prick, according to the manufacturer's specifications. The profile includes measurements of total cholesterol (TC), HDL, TC:HDL ratio, plasma triglyceride concentration (TRG), and glucose (Glu), with a calculation for LDL using the Friedewald formula (1) (Friedewald et al. 1972):

$$\mathrm{LDL} = \mathrm{TC} - \mathrm{HDL} - (\mathrm{TRG}/5) \quad (1)$$

VO_{2max} and $V_{VO_{2max}}$

Each participant completed an incremental exercise test on a motorized treadmill (Woodway USA, Waukesha, WI) to determine VO_{2max} using a metabolic measuring system (ParvoMedics, East Sandy, UT), $V_{VO_{2max}}$, and maximal heart rate (Polar Electro Inc., Lake Success, NY). The protocol consisted of four 3 min stages with speeds increasing by 0.81 km h^{-1} at each stage. If the fourth stage was completed, then the incline was increased 2 % every min until VO_{2max} was reached. If no plateau in VO_2 was reached at the end of the test, then 2 of the following criteria were met in order to consider it a valid test: (1) heart rate within 10 beats of age-predicted max ($207 - 0.7 \times$ age), (2) respiratory exchange ratio >1.15, or (3) volitional exhaustion. Values were measured every 15 s and averaged for each minute. For the safety of the participants, if $V_{VO_{2max}}$ was not determined in the first four stages of the incremental exercise test, then it was estimated by extrapolating the relationship between speed and VO_2 over the first four stages. The average correlation between speed and VO_2 over the four submaximal stages used to estimate $V_{VO_{2max}}$ was $r^2 = 0.9839$.

Training

The total duration of exercise training for both groups was matched, lasting 30 min per day, 3 days per week for 8 weeks. Both groups also exercised at the same average relative intensity on each day, which included a 3 min warm-up and 3 min cool-down at 60 % $V_{VO_{2max}}$. The average workload of training was approximately 1075 ± 181 kcal $week^{-1}$ for weeks 1–2, 1139 ± 191 kcal $week^{-1}$ for weeks 3–4, 1215 ± 185 kcal $week^{-1}$ for weeks 5–6, and 1282 ± 195 kcal $week^{-1}$ for weeks 7–8.

The ET group ran at a constant pace each training day, with the intensity set to 70 % of $V_{VO_{2max}}$ for weeks 1–2, 75 % of $V_{VO_{2max}}$ for weeks 3–6, and 80 % of $V_{VO_{2max}}$ for weeks 7–8. The HIIT group completed 12 intervals, at a ratio of 1 min work to 1 min active recovery. During weeks 1–2, the intervals were 1 min at 90 % of $V_{VO_{2max}}$ and 1 min at 50 % of $V_{VO_{2max}}$. For weeks 3–6, the intensity increased to 1 min at 100 % of $V_{VO_{2max}}$ and 1 min at 50 % of $V_{VO_{2max}}$, and for weeks 7–8 the intensity again increased to 1 min at 110 % $V_{VO_{2max}}$ and 1 min at 50 % of $V_{VO_{2max}}$. The average $V_{VO_{2max}}$ used to generate exercise protocols at the start of the study was 12.07 ± 0.81 km h^{-1} for the HIIT group and 11.91 ± 1.93 km h^{-1} for the ET group ($p = 0.88$). All training sessions were completed on laboratory treadmills programmed with each participant's training protocol and supervised by a researcher trained in adult CPR/AED. Participants were also instructed to maintain their normal diet and daily activities throughout the duration of the study.

Statistical analysis

This study employed a within-individual and between-groups design using matched groups, based on initial HDL concentration and VO_{2max}. If the baseline values were normally distributed, then t tests were used to determine if there were any significant initial differences between the two groups. For nonparametric baseline values, a Wilcoxon–Mann–Whitney test was used to evaluate any potential baseline differences. Normality was determined by the Shapiro–Wilk normality test. Two-way repeated-measures ANOVAs were used to examine main effects for training and group on differences in adaptations for data that did not violate assumptions of normality. For nonparametric data, the Wilcoxon sign rank test was used for within-subjects analysis, and the Friedman ranked ANOVA for nonparametric data was used for between-groups analysis. Outliers were included in the analysis unless they were greater than ±3 standard deviations away from the mean and exhibited undue influence on the results. Significance was set a priori

to $\alpha = 0.05$. SAS 9.3 (SAS Institute Inc., Cary, NC) was used to complete all statistical analyses in this study.

Results

All 12 participants included in the analysis completed the 8 weeks of exercise training in the study with an adherence rate of 100 %. There were no adverse events during any of the training sessions, and no injuries were incurred as a direct result of participating in the study.

Inflammation

Data for CRP and IL-6 concentrations violated assumptions of normality and were thus analyzed using the Wilcoxon sign rank test and the Friedman ranked ANOVA for nonparametric data. CRP concentrations were not different at baseline between groups ($p = 0.23$) and were not significantly altered by either HIIT (5.12 ± 4.30 vs. 5.50 ± 3.61 ng mL, $p = 0.84$) or ET (22.41 ± 26.09 vs. 15.46 ± 11.30 ng mL, $p = 0.84$), with no significance difference in adaptation between groups ($p = 0.88$) (Fig. 2). The plasma IL-6 concentration was not significantly elevated immediately after exercise for either running protocol on either the first (HIIT −0.09 ± 0.48 ng mL^{-1}; ET −1.99 ± 4.00 ng mL^{-1}) or the last exercise day (HIIT 5.92 ± 9.14 ng mL^{-1}; ET 0.70 ± 2.21 ng mL^{-1}) (Fig. 1). The IL-6 response to exercise was no different after the 8 weeks of training (HIIT $p = 0.22$; ET $p = 0.84$), and was not significantly different between groups ($p = 0.45$).

Lipid profile

In the ET group, there was an outlier in the results for TRG concentration, greater than ±3 standard deviations from the mean and causing a nonparametric distribution of the data. Therefore the pre- and post-training TRG results for that participant were excluded from the analysis. The plasma TRG concentration was significantly reduced only in the HIIT group, with the magnitude of change significantly different from that seen in the ET group. However, the TC:HDL ratio was significantly lowered only in the ET group, though this difference was not significantly different from the HIIT group. The changes in HDL, LDL, TC, and Glu concentrations did not reach significance in either group and were not significantly different between groups (Table 2).

Body composition

After the 8 weeks of exercise training, the ET group had significantly reduced the percentage of android fat from 36.78 ± 9.60 to 34.18 ± 11.39 % ($p = 0.046$). There was no significant difference in the HIIT group (34.98 ± 8.23–33.13 ± 9.87 %, $p = 0.24$) and no significant difference between the groups ($p = 0.67$). There were no significant differences within- or between-groups for changes in weight (HIIT 81.9 ± 10.0–80.6 ± 9.5 kg, $p = 0.24$; ET 90.2 ± 21.1–90.6 ± 21.9 kg, $p = 0.65$; between-groups $p = 0.21$), percent fat (HIIT 28.23 ± 7.03–27.32 ± 7.66 %, $p = 0.21$; ET 27.90 ± 7.97–26.37 ± 9.01 %, $p = 0.10$; between-groups $p = 0.55$), or gynoid fat (HIIT 33.97 ± 6.45–33.97 ± 7.38 %, $p = 1.00$; ET 32.15 ± 7.63–31.13 ± 8.43 %, $p = 0.55$, between-groups $p = 0.55$) (Fig. 3). Training also did not result in any significant changes in lean mass (HIIT 24.1 ± 4.4–26.3 ± 8.1 kg, $p = 0.54$; ET 32.0 ± 10.2–31.3 ± 10.9 kg, $p = 0.93$).

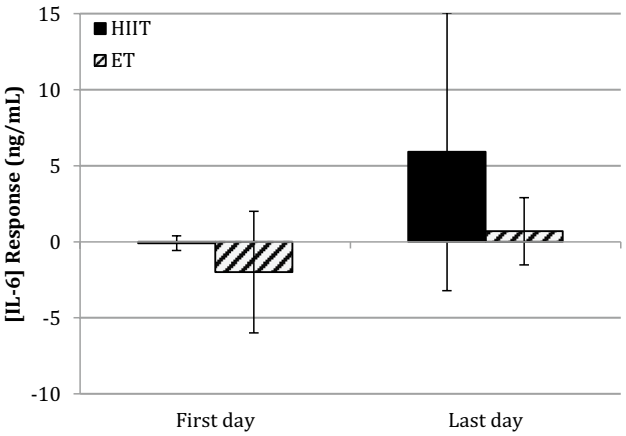

Fig. 1 IL-6 response to exercise on the first and last training days. Data violated assumptions of normality. No significant differences found within- or between-groups

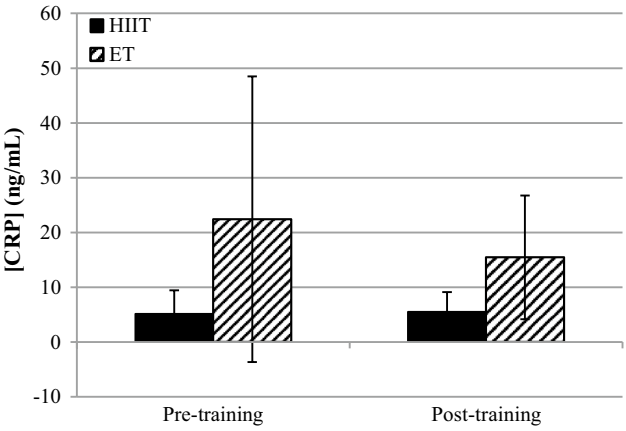

Fig. 2 CRP concentrations before and after the training period. Data violated assumptions of normality. No significant differences found within- or between-groups

Table 2 Lipid and glucose measures before and after training

	HIIT pre	HIIT post	ET pre	ET post
TC (mg dL^{-1})	140 ± 17	143 ± 24	155 ± 22	159 ± 24
HDL (mg dL^{-1})	34 ± 9	40 ± 9	34 ± 8	41 ± 10
LDL (mg dL^{-1})	88 ± 17	92 ± 28	101 ± 15	99 ± 17
TC:HDL (mg dL^{-1})	4.37 ± 1.39	3.85 ± 1.29	4.67 ± 0.85	4.07 ± 0.96*
TRG (mg dL^{-1})	92 ± 32	61 ± 12*#	87 ± 36	99 ± 17
Glu (mg dL^{-1})	89 ± 6	90 ± 8	87 ± 7	92 ± 5

All values are presented as mean ± SD

* Significantly different within-groups

Significantly different between-groups

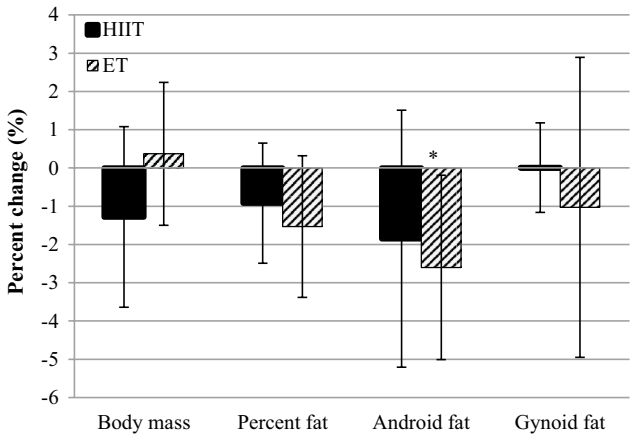

Fig. 3 Body composition before and after training. *Significantly different within-group ($p < 0.05$)

VO_{2max}

There was no significant difference in baseline VO_{2max} between the groups (Table 1), and the training period did not result in any significant difference in VO_{2max}, either within (HIIT 41.5 ± 5.5 vs. 44.1 ± 6.8 mL kg^{-1} min^{-1}, $p = 0.13$; ET 41.9 ± 5.8 vs. 43.5 ± 7.2 mL kg^{-1} min^{-1}, $p = 0.31$) or between groups ($p = 0.62$).

Discussion

The primary findings of this study were that this HIIT protocol reduced plasma TRG concentrations, a response that was significantly different from the TRG response to ET, in sedentary young men, but only ET significantly improved the TC:HDL ratio and reduced the percentage of android fat. Plasma concentrations of TRG are an independent risk factor for future cardiovascular incidents (Hokanson and Austin 1996). The response of plasma TRG concentrations to general exercise training is varied, with factors such as initial TRG concentration and initial HDL concentration possibly playing a role in the response (Couillard et al. 2001). The response of plasma TRG specifically to HIIT is also varied, with some studies in agreement with our results, finding significantly reduced TRG concentrations (Wisløff et al. 2007), but others have found plasma TRG responses that were not significant (Helgerud et al. 2007; Tjønna et al. 2008). One potential source for these differences could be differences in HIIT protocol employed, since HIIT protocols can be generated with nearly infinite combinations of training variables, some of which likely result in different physiological stressors and adaptations (Stepto et al. 1999). Though not measured, the reduction of plasma TRG could be indicative of increased lipoprotein lipase (LPL) enzyme activity, as the two are inversely associated (Blades et al. 1993). However, LPL not only plays a role in the breakdown of triglycerides, but is also directly associated with HDL concentration through its involvement in the maturation of HDL molecules, adding additional apolipoprotein A-1 subunits to HDL (Lewis and Rader 2005). This enzyme is secreted from metabolically active tissue, so it is not unreasonable to speculate that greater peaks in metabolic rate during high intensity intervals could result in greater LPL release than during ET, even when average intensity and duration are matched. But this speculation is weakened by the fact that HDL concentrations were not increased as a result of either of the training protocols employed. Based on the limited evidence available, it seems a satisfactory mechanism cannot be suggested at this time.

Conversely, the TC:HDL ratio, which is a better predictor of CHD and insulin resistance than the LDL:HDL ratio (Lemieux et al. 2001), was significantly reduced only in the ET group, with no significant reduction in the HIIT group. These results are similar to those seen by Nybo et al. (2010), in which moderate ET significantly reduced the TC:HDL ratio. It is worth mentioning that the Nybo et al. results cannot be directly compared to our study, due to distinct differences in training protocols, such as mismatched

workloads between their interval training and moderate training groups. Regardless, it does appear that ET is more beneficial than HIIT for improving the TC:HDL ratio.

While no change in body composition was expected due to the lack of a dietary intervention, we found that the percentage of android fat was significantly reduced only in the ET group. This finding contradicts the general pattern of findings in the literature, in which HIIT is shown to be more effective for reducing total body mass as well as percentages of android fat (Boutcher 2011). One potential source of this disparity could be the difference in HIIT and ET protocols used this study compared to previous research, as our moderate ET was more intense (~75 % $V_{VO_{2max}}$) than the steady-state exercise protocols previously used (60 % VO_{2max}) (Trapp et al. 2008). Another potential factor is altered dietary habits of the participants Although the participants were instructed to maintain their normal diets and none reported any notable dietary changes over the course of the study, diet was self-reported and not controlled directly by the researchers. It is possible that engaging in an 8-week training program resulted in subconscious dietary or lifestyle changes, though if this did happen it was not noticed by the participants or the researchers.

Android fat has been shown to be a significant independent predictor of CHD in middle-aged men and to be strongly correlated with cardiovascular risk factors in children and adolescents (Casassus et al. 1992; Daniels et al. 1999). Reductions in android fat in young, healthy, sedentary men through moderate ET has important implications for the prevention of CHD through a lifetime of regular physical activity. Based on these limited results from our relatively small sample size, it appears that exercise programs aimed at reducing the risk of CHD events should potentially include traditional moderate intensity exercise as well as HIIT.

Increases in the concentration of HDL in both the HIIT and ET groups (16 and 19 %, respectively) did not reach significance (HIIT $p = 0.33$; ET $p = 0.08$). However, the magnitude of increase was very similar to the significant increase (18 %, $p < 0.05$) measured by Musa et al. in a study that used a nearly identical training stimulus as our HIIT group: 8 weeks of HIIT 3 days per week, with work interval intensities of 90 % of VO_{2max}, a 1:1 work to rest ratio, and an energy expenditure of 1269 kcal week^{-1} (Musa et al. 2009). Farrell and Barboriak (1980) also found significant increases in HDL concentration (7 %) after 8 weeks of exercise training 3–4 days per week at an average intensity of 70 % of VO_{2max}. Measuring HDL every week, they found a decrease in HDL concentration over the first 2 weeks, followed by a linear 1 mg dL^{-1} wk^{-1} increase in HDL over the next 6 weeks. While we only measured HDL concentration before and after the 8 weeks of training and the changes were not significant, our results appear to follow (or at least do not contradict) this pattern, with participants averaging a 6 mg dL^{-1} increase over the 8 weeks.

Interestingly, neither training protocol used in this study resulted in significant reductions in resting CRP concentrations, despite the fact that our initially sedentary participants averaged an energy expenditure of approximately 1075–1282 kcal week^{-1}, when previous research shows that only 200–599 kcal of exercise per week is sufficient to reduce CRP, and that further reductions occur when energy expenditure is increased to 600–1499 kcal week^{-1} (Mora et al. 2007). Reduced chronic inflammation is potentially the result of adaptations to repeated inflammatory challenges arising from regular exercise, which is seen in the acute phase response of plasma IL-6 (Mattusch et al. 2000). This acute inflammatory response is common in the literature (Starkie et al. 2001), having been measured in high-intensity exercise lasting as short as 6 min (Nielsen et al. 1996). Although our HIIT protocol consisted of 12 total minutes near, at, or above $V_{VO_{2max}}$, we did not detect a significant acute phase response of IL-6 on either the first or final day of training.

The plasma concentration of IL-6 is increased when the energy demand from carbohydrate metabolism cannot be met due to some limitation during exercise, usually glycogen depletion (Saltin and Karlsson 1971; Karlsson and Saltin 1971). Therefore, HIIT has the potential to result in greater IL-6 increases than work-matched moderate ET, as it relies more heavily on carbohydrate oxidation than ET when workloads are matched (Malatesta et al. 2009). The relationship between carbohydrate metabolism capability and IL-6 response may explain how chronic exercise training can result in a blunted acute inflammatory response, despite increases in the absolute workload of an exercise session (Croft et al. 2009). This adaptive response may be a result of increased glycogen storage and a reduced reliance on carbohydrate metabolism, both of which may occur after a period of HIIT (Burgomaster et al. 2006).

Several different HIIT protocols have been shown to significantly reduce muscle glycogen content, including 30 s Wingate sprints (Bogdanis et al. 1996), 1 min intervals at 130 % $V_{VO_{2max}}$ (Krustrup et al. 2004), and 5 min intervals at 85 % of VO_{2max} (Stepto et al. 2001). The studies mentioned are not easily compared due to differences in the training status of the populations examined. However, if acute increases in IL-6 are driven by the inhibition of carbohydrate utilization that accompanies glycogen depletion, then seeking a HIIT protocol that results in the greatest glycogen reduction and acute increases in inflammation, leading to chronic decreases in inflammation, would be beneficial. Acute increases in IL-6 are intensity dependent (Ostrowski et al. 2000), but when the intensity of exercise is normalized, the IL-6 response to increased exercise duration is exponential, with small increases in time resulting in large

increases in IL-6 (Fischer 2006). The interplay between intensity and work interval duration need to be carefully considered in future studies examining this topic.

The results of this study indicate that while 8 weeks of exercise training can reduce the risk of future CHD events by significantly improving TRG concentrations (HIIT) and the TC:HDL ratio (ET), it may not provide a more anti-inflammatory environment necessary to improve the functional ability of HDL in sedentary, but healthy, young men. These results should be viewed cautiously, as our small sample size prevents any broad generalizations from being made. However, previous research has shown this adaptation to be possible in diseased populations. Roberts et al. (2006) witnessed improvements in the anti-inflammatory role of HDL after only 3 weeks of training and dietary intervention in patients at risk for metabolic syndrome, but their participants exercised daily for 3 weeks for 45–60 min per session at an intensity of 70–85 % of HR_{max}. Iborra et al. (2008) also demonstrated increased anti-inflammatory HDL function in middle-aged participants with diabetes mellitus and low aerobic fitness ($VO_{2max} = 17.8$ mL kg^{-1} min^{-1}) after 18 weeks of exercise training at similar intensities to this study. The reductions in CRP found in both of these two studies also support a previously demonstrated association between increases in physical fitness, decreases in CRP, and increases in HDL function (Mattusch et al. 2000; Mora et al. 2007).

Conclusions

This study demonstrates that risk factors for future CHD events can be significantly reduced in young, healthy, sedentary males in just 8 weeks by high intensity interval training or moderate intensity ET. Due to the differences in response, with HIIT improving TRG concentrations and ET improving the TC:HDL ratio and reducing android fat, it is likely that both types of training warrant inclusion in an exercise training regimen. However, the HIIT and ET protocols used in this study did not induce an acute inflammatory response or decrease chronic inflammation, indicating that these responses to exercise training may not be as common as the literature has previously suggested.

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Compliance with ethical standards

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Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

Ansell BJ, Navab M, Hama S et al (2003) Inflammatory/antiinflammatory properties of high-density lipoprotein distinguish patients from control subjects better than high-density lipoprotein cholesterol levels and are favorably affected by simvastatin treatment. Circulation 108:2751–2756. doi:10.1161/01.CIR.0000103624.14436.4B

Aronson D, Sheikh-Ahmad M, Avizohar O et al (2004) C-reactive protein is inversely related to physical fitness in middle-aged subjects. Atherosclerosis 176:173–179. doi:10.1016/j.atherosclerosis.2004.04.025

Blades B, Vega GL, Grundy SM (1993) Activities of lipoprotein lipase and hepatic triglyceride lipase in postheparin plasma of patients with low concentrations of HDL cholesterol. Arterioscler Thromb Vasc Biol 13:1227–1235. doi:10.1161/01.ATV.13.8.1227

Bogdanis GC, Nevill ME, Boobis LH, Lakomy HK (1996) Contribution of phosphocreatine and aerobic metabolism to energy supply during repeated sprint exercise. J Appl Physiol 80:876–884

Boutcher SH (2011) High-intensity intermittent exercise and fat loss. J Obes 2011:868305. doi:10.1155/2011/868305

Burgomaster KA, Heigenhauser GJF, Gibala MJ (2006) Effect of short-term sprint interval training on human skeletal muscle carbohydrate metabolism during exercise and time-trial performance. J Appl Physiol 100:2041–2047. doi:10.1152/japplphysiol.01220.2005

Burgomaster KA, Howarth KR, Phillips SM et al (2008) Similar metabolic adaptations during exercise after low volume sprint interval and traditional endurance training in humans. J Physiol 586:151–160. doi:10.1113/jphysiol.2007.142109

Casassus P, Fontbonne A, Thibult N et al (1992) Upper-body fat distribution: a hyperinsulinemia-independent predictor of coronary heart disease mortality. The Paris Prospective Study. Arterioscler Thromb Vasc Biol 12:1387–1392. doi:10.1161/01.ATV.12.12.1387

Couillard C, Despres J-P, Lamarche B et al (2001) Effects of endurance exercise training on plasma HDL cholesterol levels depend on levels of triglycerides: evidence from men of the Health, Risk Factors, Exercise Training and Genetics (HERITAGE) Family Study. Arterioscler Thromb Vasc Biol 21:1226–1232. doi:10.1161/hq0701.092137

Croft L, Bartlett JD, MacLaren DPM et al (2009) High-intensity interval training attenuates the exercise-induced increase in plasma IL-6 in response to acute exercise. Appl Physiol Nutr Metab 34:1098–1107. doi:10.1139/H09-117

Cullinane EM, Yurgalevitch SM, Saritelli AL et al (1995) Variations in plasma volume affect total and low-density lipoprotein cholesterol concentrations during the menstrual cycle. Metabolism 44:965–971. doi:10.1016/0026-0495(95)90090-X

Daniels SR, Morrison JA, Sprecher DL et al (1999) Association of body fat distribution and cardiovascular risk factors in children and adolescents. Circulation 99:541–545. doi:10.1161/01.CIR.99.4.541

Demacker PNM, Schade RWB, Stalenhoef AFH et al (1982) Influence of contraceptive pill and menstrual cycle on serum lipids

and high-density lipoprotein cholesterol concentrations. Br Med J 284:1213–1215. doi:10.1136/bmj.284.6324.1213
Farrell PA, Barboriak J (1980) The time course of alterations in plasma lipid and lipoprotein concentrations during eight weeks of endurance training. Atherosclerosis 37:231–238. doi:10.1016/0021-9150(80)90008-8
Fischer CP (2006) Interleukin-6 in acute exercise and training: what is the biological relevance? Exerc Immunol Rev 12:6–33
Friedewald WT, Levy RI, Fredrickson DS (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 18:499–502
Gordon T, Castelli WP, Hjortland MC et al (1977) High density lipoprotein as a protective factor against coronary heart disease. Am J Med 62:707–714. doi:10.1016/0002-9343(77)90874-9
Helgerud J, Høydal K, Wang E et al (2007) Aerobic high-intensity intervals improve VO2max more than moderate training. Med Sci Sports Exerc 39:665–671. doi:10.1249/mss.0b013e3180304570
Hellsten Y, Apple F, Sjödin B (1996) Effect of sprint cycle training on activities of antioxidant enzymes in human skeletal muscle. J Appl Physiol 81:1484–1487
Hickson RC, Hagberg JM, Ehsani AA, Holloszy JO (1981) Time course of the adaptive responses of aerobic power and heart rate to training. Med Sci Sports Exerc 13:17–20
Hokanson JE, Austin MA (1996) Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. J Cardiovasc Risk 3:213–219. doi:10.1177/174182679600300214
Iborra RT, Ribeiro ICD, Neves MQTS et al (2008) Aerobic exercise training improves the role of high-density lipoprotein antioxidant and reduces plasma lipid peroxidation in type 2 diabetes mellitus. Scand J Med Sci Sports 18:742–750. doi:10.1111/j.1600-0838.2007.00748.x
Karlsson J, Saltin B (1971) Diet, muscle glycogen, and endurance performance. J Appl Physiol 31:203–206
Krustrup P, Hellsten Y, Bangsbo J (2004) Intense interval training enhances human skeletal muscle oxygen uptake in the initial phase of dynamic exercise at high but not at low intensities. J Physiol 559:335–345. doi:10.1113/jphysiol.2004.062232
Leggate M, Nowell MA, Jones SA, Nimmo MA (2010) The response of interleukin-6 and soluble interleukin-6 receptor isoforms following intermittent high intensity and continuous moderate intensity cycling. Cell Stress Chaperones 15:827–833. doi:10.1007/s12192-010-0192-z
Lemieux I, Lamarche B, Couillard C et al (2001) Total cholesterol/HDL cholesterol ratio vs LDL cholesterol/HDL cholesterol ratio as indices of ischemic heart disease risk in men. Arch Intern Med 161:2685–2692. doi:10.1001/archinte.161.22.2685
Lewis GF, Rader DJ (2005) New insights into the regulation of HDL metabolism and reverse cholesterol transport. Circ Res 96:1221–1232. doi:10.1161/01.RES.0000170946.56981.5c
Lindhorst E, Young D, Bagshaw W (1997) Acute inflammation, acute phase serum amyloid A and cholesterol metabolism in the mouse. Biophys Acta. doi:10.1016/S0167-4838(96)00227-0
Malatesta D, Werlen C, Bulfaro S et al (2009) Effect of high-intensity interval exercise on lipid oxidation during postexercise recovery. Med Sci Sports Exerc 41:364–374. doi:10.1249/MSS.0b013e3181857edo
Mattusch F, Dufaux B, Heine O et al (2000) Reduction of the plasma concentration of C-reactive protein following nine months of endurance training. Int J Sports Med 21:21–24. doi:10.1055/s-2000-8852
Meckel Y, Eliakim A, Seraev M et al (2009) The effect of a brief sprint interval exercise on growth factors and inflammatory mediators. J Strength Cond Res 23:225–230
Mora S, Cook N, Buring JE et al (2007) Physical activity and reduced risk of cardiovascular events: potential mediating mechanisms. Circulation 116:2110–2118. doi:10.1161/CIRCULATIONAHA.107.729939
Musa DI, Adeniran SA, Dikko AU, Sayers SP (2009) The effect of a high-intensity interval training program on high-density lipoprotein cholesterol in young men. J Strength Cond Res 23:587–592. doi:10.1519/JSC.0b013e318198fd28
Nielsen HB, Secher NH, Christensen NJ, Pedersen BK (1996) Lymphocytes and NK cell activity during repeated bouts of maximal exercise. Am J Physiol Regul Integr Comp Physiol 271:R222–R227
Nybo L, Sundstrup E, Jakobsen MD et al (2010) High-intensity training versus traditional exercise interventions for promoting health. Med Sci Sports Exerc 42:1951–1958. doi:10.1249/MSS.0b013e3181d99203
Ostrowski K, Schjerling P, Pedersen BK (2000) Physical activity and plasma interleukin-6 in humans—effect of intensity of exercise. Eur J Appl Physiol 83:512–515. doi:10.1007/s004210000312
Ridker PM, Hennekens CH, Buring JE, Rifai N (2000) C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med 342:836–843. doi:10.1056/NEJM200003233421202
Roberts CK, Won D, Pruthi S et al (2006) Effect of a short-term diet and exercise intervention on oxidative stress, inflammation, MMP-9, and monocyte chemotactic activity in men with metabolic syndrome factors. J Appl Physiol 100:1657–1665. doi:10.1152/japplphysiol.01292.2005
Saltin B, Karlsson J (1971) Muscle glycogen utilization during work of different intensities. In: Pernow B, Saltin B (eds) Muscle metabolism during exercise. Springer, Boston, pp 289–299
Starkie RL, Arkinstall MJ, Koukoulas I et al (2001) Carbohydrate ingestion attenuates the increase in plasma interleukin-6, but not skeletal muscle interleukin-6 mRNA, during exercise in humans. J Physiol 533:585–591. doi:10.1111/j.1469-7793.2001.0585a.x
Stepto NK, Hawley JA, Dennis SC, Hopkins WG (1999) Effects of different interval-training programs on cycling time-trial performance. Med Sci Sports Exerc 31:736–741. doi:10.1097/00005768-199905000-00018
Stepto NK, Martin DT, Fallon KE, Hawley JA (2001) Metabolic demands of intense aerobic interval training in competitive cyclists. Med Sci Sports Exerc 33:303–310. doi:10.1097/00005768-200102000-00021
Tjønna AE, Lee SJ, Rognmo Ø et al (2008) Aerobic interval training versus continuous moderate exercise as a treatment for the metabolic syndrome: a pilot study. Circulation 118:346–354. doi:10.1161/CIRCULATIONAHA.108.772822
Trapp EG, Chisholm DJ, Freund J, Boutcher SH (2008) The effects of high-intensity intermittent exercise training on fat loss and fasting insulin levels of young women. Int J Obes (Lond) 32:684–691. doi:10.1038/sj.ijo.0803781
VanLenten BJ, Hama SY, de Beer FC et al (1995) Anti-inflammatory HDL becomes pro-inflammatory during the acute phase response. Loss of protective effect of HDL against LDL oxidation in aortic wall cell cocultures. J Clin Invest 96:2758–2767. doi:10.1172/JCI118345
Whaley MH, Brubaker PH, Otto RM, Armstron LE (2006) ACSM's guidelines for exercise testing and prescription, 7th edn. Lippincott Williams & Wilkins, Philadelphia
Wisløff U, Støylen A, Loennechen JP et al (2007) Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. Circulation 115:3086–3094. doi:10.1161/CIRCULATIONAHA.106.675041