Title: Effects of 12 weeks of high intensity intermittent exercise training on appetite regulation in overweight men.

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Running head: Exercise training and appetite regulation
Abstract

Objective: An acute bout of high intensity intermittent exercise suppresses ad-libitum energy intake at the post-exercise meal. The present study examined the effect of 12 weeks of high intensity intermittent exercise training (HIIT) compared with moderate intensity continuous exercise training (MICT) on appetite regulation.

Methods: Thirty overweight, inactive men (BMI: 27.2 ± 1.3 kg/m²; $\overline{V}O_2$Peak: 35.3 ± 5.3 mL.kg⁻¹.min⁻¹) were randomised to either HIIT or MICT (involving 12 weeks of training, 3 sessions per week) or a control group (CON) (n = 10 per group). Ad-libitum energy intake from a laboratory test meal was assessed following both a low-energy (LEP: 1590 kJ) and a high-energy preload (HEP: 2413 kJ) pre and post-intervention. Perceived appetite and appetite-related blood variables also were measured.

Results: There was no significant effect of the intervention period on energy intake at the test meal following the two different preloads (p ≥ 0.05). However, the 95% CI indicated a clinically meaningful decrease in energy intake after the HEP compared with LEP in response to HIIT (516 ± 395 kJ), but not MICT or CON, suggesting improved appetite regulation. This was not associated with alterations in the perception of appetite or the circulating concentration of a number of appetite-related peptides or metabolites, although insulin sensitivity was enhanced with HIIT only (p = 0.003).

Conclusion: HIIT appears to benefit appetite regulation in overweight men. The mechanisms for this remain to be elucidated.

Keywords: Energy intake, Insulin sensitivity,
Introduction

A growing body of research has demonstrated a link between exercise and the physiological mechanisms controlling appetite and energy intake; with inactivity potentially contributing to a positive energy balance and subsequent weight gain (18, 21, 29). Conversely, it is widely acknowledged that exercise plays a prominent role in weight management by i) contributing to a negative energy balance by increasing energy expenditure (3, 4, 26) and ii) having a favourable influence on the sensitivity of appetite regulation (24), the total amount of energy consumed (28), feelings of hunger and fullness (3, 9) as well as the circulating levels of a number of appetite-related hormones (1, 3).

More specifically, Martins and colleagues (24) demonstrated that six weeks of moderate intensity aerobic exercise training (4 sessions per week, at ~65–75% of maximum heart rate) improved appetite regulation in previously inactive, normal weight individuals by promoting more sensitive eating behaviour in response to previous energy intake. Similar improvements in appetite regulation have been reported in inactive, overweight participants in response to 12 weeks of aerobic exercise training (5 sessions per week, at ~75% of maximum heart rate; (23). However, there is evidence that the benefits of exercise training for appetite-regulation may be optimised by manipulating the specific type of exercise employed. For instance, Guelfi and colleagues (9) found that 12 weeks (3 sessions per week) of aerobic based exercise training (stationary cycling and elliptical cross training at ~70-80% of maximum heart rate) increased both fasting and postprandial ratings of perceived fullness, while an equivalent period of resistance training (machine and free weights) did not.

Another important aspect of exercise prescription that may influence appetite-regulation is the intensity of training. Support for this notion comes from a recent study by our lab showing that an acute bout of intermittent high-intensity exercise (consisting of repeated
bouts of 15-s at ∼170% \( \dot{V}O_2\text{Peak} \) with an active recovery period of 60-s at ∼32% \( \dot{V}O_2\text{Peak} \)

attenuates energy intake in the post-exercise meal compared with a bout of continuous moderate intensity exercise (∼60% \( \dot{V}O_2\text{Peak} \)) of matched total work and a resting control in overweight and inactive men (28). The lower energy intake following intermittent exercise was associated with reduced active ghrelin, together with elevated blood lactate and glucose.

Additionally, free-living energy intake in the 48 h after leaving the laboratory remained lower after the intermittent exercise compared with moderate exercise and control. Whether these acute benefits of intermittent high-intensity exercise translate to differences in long-term appetite-regulation and weight loss remains to be determined. Therefore, the purpose of the present study was to examine the effect of 12-weeks of supervised exercise (intermittent high-intensity exercise [HIIT] compared with continuous moderate intensity [MICT] and a no-exercise control) on appetite regulation (using the high energy versus low energy preload test meal paradigm), perceptions of appetite and the circulating concentrations of appetite-related hormones (in particular active ghrelin, leptin, insulin, pancreatic peptide (PP), peptide tyrosine tyrosine (PYY)) in the fasted state and in response to caloric consumption in previously inactive, overweight men. It was hypothesised that 12 weeks of supervised exercise would improve appetite regulation (i.e. promote more sensitive eating behaviour) compared with a no-exercise control, but that the improvement would be of a greater extent in response to HIIT compared with MICT.

**Methods**

**Participants**

Thirty overweight, physically inactive men (age 31± 8 yr; BMI 27.2 ± 1.3 kg/m²; \( \dot{V}O_2\text{Peak} \): 35.3 ± 5.3 mL.kg\(^{-1}\).min\(^{-1}\)) were recruited from the local community. Physical inactivity was defined as not engaging in moderate intensity exercise for more than 75 min per week (33).
To minimise any influence of dietary restraint on the results, participants were excluded if they scored \( \geq 3.5 \) on the restraint scale of the Dutch Eating Behaviour Questionnaire (DEBQ) (31). Ethics approval was granted by the Human Research Ethics Committee at The University of Western Australia and written consent was obtained from all participants.

**Study design**

Participants were randomly allocated (using a random number generator software (30) into one of three experimental groups; i) HIIT, ii) MICT, or iii) control - no exercise training (CON). Appetite regulation was assessed pre- and post-intervention using a preload-test meal protocol (involving the assessment of *ad-libitum* energy intake in response to previous energy intake of differing caloric content). The effect of the intervention period on perceived appetite, appetite-related blood variables, free-living energy intake, physical activity levels, anthropometrical measures, aerobic fitness, dietary restraint and physical activity enjoyment were also assessed.

**Baseline testing and familiarisation**

Participants completed an initial baseline testing and familiarisation session. This included the assessment of i) body composition using Dual-energy X-ray absorptiometry (GE Lunar Prodigy Vision, GE Medical Systems, Madison, WI, USA), ii) peak aerobic capacity (\( \dot{V}O_{2\text{Peak}} \)) using a continuous incremental exercise test performed on an air-braked cycle ergometer as previously described (28) and iii) dietary restraint via the DEBQ (31). Familiarisation with the questionnaires and protocols to be used for the subsequent assessment of pre- and post-intervention outcome measures (i.e. blood sampling, laboratory test meal) was also performed during this session to minimise the novelty of these tasks. Body composition, peak aerobic capacity and dietary restraint were re-assessed at the end of the study period.
Pre- and post-intervention testing

Participants attended the laboratory at approximately 0700 h, having fasted for 10-12 h, on two separate occasions both pre- and post-intervention (i.e. four visits in total) for the assessment of outcomes measures. In the 24 h prior to each trial, participants were required to document their food and drink consumption and to refrain from vigorous physical activity. Enjoyment of physical activity was assessed pre- and post-intervention (i.e. first and final exercise training session) via the Physical Activity Enjoyment Scale (PACES) (16).

Preload test meal

Upon arrival to the laboratory, participants were provided with either a high energy (HEP; 2438 kJ) or low energy preload (LEP; 847 kJ) in a counterbalanced, single blind design (preloads were of similar volume and sensory properties for consumption). The HEP consisted of 250 ml Up & Go® liquid breakfast (Sanitarium™, Berkeley Vale, NSW, Australia), 100 g Maltodextrin (Poly-Joule®, Nutricia, Macquarie Park, NSW, Australia) and ~100 ml of water to make a total volume of 450 ml, while the LEP consisted of 250 ml Up & Go® liquid breakfast, 2 g of ThickenUp™ Clear, Resource®, Nestlé, Notting Hill, VIC, Australia, 5 ml Sugarless® Liquid Sweetener, (Sugarless™, Chipping Norton, NSW, Australia) and ~193 ml water to make a total volume of 450 ml.

Participants remained seated for 70 min after consuming the preload, at which point they were given access to a laboratory test meal for 20 min during which time they were instructed to consume *ad-libitum* until they felt “comfortably full”. The test meal consisted of porridge made from a mixture of instant oats (Oats Quick Sachet – Creamy Honey, Uncle Tobys®, Nestlé, Rhodes, NSW, Australia) and milk (HiLo Milk, Pura®, Melbourne, VIC, Australia) of known quantity and nutrition content. A standardised bottle of plain drinking water (~1000 ml) was also available. The porridge and drinking water were weighed before and re-weighed
after consumption. Measures were taken to minimise the influence of environmental factors on eating behaviour as previously described (28).

Assessment of perceptions of appetite

Subjective perceptions of appetite (fullness, hunger, satiation, desire to eat and prospective food consumption) were assessed using a 100 mm visual analogue scale (VAS) (13) in the fasted state (before preload consumption) and in response to caloric consumption (immediately, 30 and 60 min post preload).

Assessment of appetite-related blood variables

Appetite-related blood variables were measured in the fasted state (before preload consumption) and in response to caloric consumption (30 min and 60 min post preload). To prepare the sampling site, the entire hand was placed into a box heated with warm air (~60 °C). Capillary blood (535 µl) was then collected from the warmed fingertip with the use of a sterile lancet (Unistick 2 Normal; Owen Mumford, Oxford, UK). Blood glucose concentration was measured using a blood gas analyzer (35 µL; ABL 735, Radiometer, Copenhagen, Denmark). The remaining blood was treated with EDTA (Microtainer Tubes with K2E (K2EDTA), BD Microtainer, Franklin Lakes, N.J., USA) and serine protease inhibitor (20 µl per 500 µl of blood; Pefabloc SC, Roche Diagnostics, Sydney, NSW, Australia) before being centrifuged at 1020 g for 10 min. Plasma obtained was stored at ~80°C and samples from the HEP were later analysed for a range of appetite-related hormones; leptin, insulin, active ghrelin, PP and PYY, using a commercially available assay kit (Milliplex Map Human Metabolic Hormone Magnetic Bead Panel; Millipore Corporation, Billerica, MA, USA).
Assessment of free-living energy intake and physical activity levels

Free-living energy intake and physical activity levels in the 24 h prior to and for the remainder of the day after leaving the laboratory sessions were assessed using a self-recorded food diary and accelerometry (GT1M Activity Monitor, ActiGraph, Florida, USA) respectively. The food diary required participants to record the portion size (weighing scales were provided to assist) and describe the food consumed. Detailed instructions on the use of the food diary, and the necessity for timely and accurate recordings after food and drink consumption were emphasised. Energy intake from food records was calculated using a commercially available software program (Foodworks; Xyris Software, Queensland, Australia). The total number of steps and estimated energy expenditure from physical activity based on accelerometry were determined using ActiLife software (ActiGraph, Florida, USA).

Exercise intervention

Both exercise training groups (HIIT and MICT) were required to participate in three training sessions each week over a 12 week period. All training was conducted on calibrated front access air-braked cycle ergometers (Model EX-10, Repco Cycle, Huntingdale, Victoria, Australia) that were interfaced with a customised software program (Cyclemax, School of Sport Science, Exercise and Health, UWA, Perth, Western Australia, Australia). Participants randomised to HIIT were required to complete repeated bouts of high-intensity exercise (15-s at a power output equivalent to $\sim 170\% \text{VO}_{2\text{Peak}}$) with an active recovery period (60-s at a power output $\sim 32\% \text{VO}_{2\text{Peak}}$) between efforts. Participants allocated to MICT exercised at a power output equivalent to 60% $\text{VO}_{2\text{Peak}}$ continuously, for the duration of each training session. Relative total work was matched between exercise protocols and the workload for each participant was determined using their individual baseline $\text{VO}_{2\text{Peak}}$ results.
All training sessions were fully supervised by an exercise physiologist (A.Y.S). Training sessions commenced with a 5 min warm-up that involved easy pedalling followed by light static/dynamic stretching of the lower limbs. Heart rate and rate of perceived exertion (RPE; Borg, 1982) were periodically measured during each exercise session. To accommodate for an increase in fitness throughout the intervention period, the workload and duration of the training sessions were progressively increased. Training workloads were adjusted based on a conservative 1% improvement in aerobic capacity per week, while duration progressed as follows: Weeks 1 to 3 (30 min), Weeks 4 to 6 (35 min), Weeks 7 to 9 (40 min) and Weeks 10 to 12 (45 min). In addition, the VO\textsubscript{2Peak} test was repeated during week 6 of the intervention and training workloads were further adjusted accordingly.

**Statistical Analysis**

Insulin sensitivity was calculated using the homeostatic model assessment (HOMA-IR) index (based on fasting blood glucose and insulin concentration) (32). Repeated-measures ANOVA were used to compare the estimated energy intake and energy expenditure for the 24 h prior to each lab visit for the assessment of outcome measures to confirm that these factors were well matched. Mixed model ANOVAs were applied to determine treatment effects for each outcome variable as follows; i) two-way (pre-vs.post-intervention*condition [HIIT, MICT, CON]) for aerobic fitness, anthropometrical measures, physical activity enjoyment and dietary restraint ii) three-way (pre-vs.post-intervention*preload [HEP vs. LEP]*condition) for energy intake at the laboratory test meal and 24h cumulative energy intake iii) four-way (pre-vs.post-intervention*preload*time [0 min, immediately post-preload, 30 min post-preload, 60 min post-preload and 90 min post-preload]*condition) for perceived appetite and iv) three way (pre-vs.post-intervention*time [0 min, 30 min post-preload and 60 min post-preload]*condition) for appetite-related hormone concentration in response to caloric intake.
The effect of the intervention and condition (HIIT, MICT, CON) on heart rate (HR) and RPE was assessed by mixed model ANOVA. *Post hoc* comparisons were conducted when appropriate. Statistical significance was accepted at a *p* value of ≤ 0.050 (SPSS version 20, IBM Corporation, Armonk, N.Y., USA). In addition, 95% confidence intervals (CI) were presented as [lower bound value, upper bound value]. Cohen’s *d* effect sizes (*d*) were also calculated for pairwise comparisons; only moderate (0.50 – 0.79) and large (> 0.80) effect sizes are reported. All results are presented as mean ± SD (standard deviation) unless otherwise indicated.

**Results**

**Training intervention**

Training attendance was similar between groups (*p* = 0.712), with 98 ± 3% (mean 35 of 36 sessions; minimum 33 sessions) compliance for HIIT, and 97 ± 4% (mean 35 of 36; minimum 33 sessions) for MICT. A main effect of condition revealed higher average HR (*p* < 0.001) and RPE (*p* = 0.034) during HIIT (HR: 158 ± 3 bpm; RPE: 14 ± 1) compared with MICT (HR: 133 ± 5 bpm; RPE: 13 ± 1). A main effect of training time-point showed that average HR (*p* < 0.001) and RPE (*p* < 0.001) increased through the course of both training interventions.

Following the 12 week study period, aerobic fitness was improved in both the HIIT and MICT groups (*p* < 0.001; Table 1) to a similar extent, but remained unchanged in the CON group. There were no significant changes in anthropometrical measures (body mass; *p* = 0.234, BMI; *p* = 0.204 and body fat; *p* = 0.187) in response to the interventions (Table 1).

With respect to the enjoyment of exercise, there was a main effect of the exercise intervention period (*p* = 0.006), with an increase in enjoyment post-intervention compared with baseline (pre-intervention 93 ± 15, post-intervention 102 ± 13 *d* = 0.64), however there was no
difference between HIIT and MICT ($p = 0.172$). There was no interaction effect of pre- vs.post-intervention*condition on dietary restraint (Pre- vs. post-intervention - HIIT: $2.7 \pm 0.4$ vs. $2.6 \pm 0.5$ MICT: $2.4 \pm 0.6$ vs. $2.5 \pm 0.8$ CON: $2.2 \pm 0.5$ vs. $2.4 \pm 0.5$; $p = 0.829$).

Ad-libitum energy intake at the laboratory test meal

Energy intake and energy expenditure from physical activity in the 24 h prior to each pre-load test session were well-matched (energy intake $p = 0.416$, energy expenditure $p = 0.768$).

Likewise, the environmental conditions were consistent during the pre-load test sessions (temperature: $21.3 \pm 0.9 \degree C$, $p = 0.996$, humidity: $52.6 \pm 7.2 \%$, $p = 0.700$).

Absolute ad-libitum energy intake at the laboratory test meal after the HEP and LEP assessed pre- and post-intervention is shown in Figure 1 and the differences in energy intake pre- to post-intervention are displayed in Table 2. Energy intake at the test meal following the two different preloads was similar at baseline in all groups ($p = 0.396$). With respect to the effect of the intervention period on energy intake from the test meals, there was no significant interaction of pre-vs.post-intervention*preload*condition ($p=0.333$), however, the 95% CI indicated a decrease in energy intake after the HEP following 12 weeks of HIIT compared with the LEP post-intervention (Table 2) suggesting a tendency for enhanced appetite regulation based on more appropriate adjustment for prior energy intake. There was no difference in ad-libitum water intake at the laboratory test meal between trials ($p = 0.601$).

Cumulative 24 h energy intake

Cumulative energy intake for the remainder of the day after the ad libitum laboratory meal is shown in Figure 2 and the differences in cumulative energy intake pre to post-intervention is presented in Table 2. Cumulative energy intake following the two different preloads was similar at baseline in all groups ($p = 0.644$). The interaction effect of pre-vs.post-intervention
preload*condition on cumulative energy intake over a 24 h period approached significance (p = 0.082).

Perception of appetite

There were no significant interactions of pre-vs.post-intervention*preload*time*condition on perceived hunger (p = 0.691), fullness (p = 0.260), satiation (p = 0.352), desire to eat (p = 0.434) or prospective food consumption (p = 0.657; results not displayed). However, there was a main effect of time within each test session for each of these variables (p < 0.001), with increased feelings of fullness and satiation, along with decreased hunger, desire to eat and prospective food consumption following the test meal.

Appetite-related blood variables

Concentrations of appetite-related blood variables assessed pre and post-intervention are shown in Figure 3. An interaction effect of pre-vs.post-intervention*time*condition was observed for insulin (p = 0.050), with post hoc analysis revealing lower insulin concentration in a fasted state following HIIT (p = 0.003 d = 0.60) and 60min after caloric consumption in MICT (p = 0.010d = 0.77) compared with pre-intervention. There was an interaction effect of pre-vs.post-intervention*condition on leptin (p = 0.017) revealing lower leptin concentration following HIIT, but not after MICT and CON. There were no interaction effects observed for active ghrelin (p= 0.736), PP (p = 0.060), PYY (p = 0.077) or blood glucose (p = 0.926). However, there was a main effect of test session time (p ≤ 0.001) for each of these blood variables, with increased PP, PYY, insulin and blood glucose in response to caloric consumption, while active ghrelin and leptin decreased over time.
There was an interaction effect of pre-vs.post-intervention*condition on HOMA-IR ($p = 0.016$), with post hoc analysis revealing significantly lower HOMA-IR following HIIT (Pre 3.8 ± 1.9, Post 2.9 ± 1.6; $p = 0.018$ $d = 0.61$) but not MICT and CON.

**Discussion**

The main aim of the present study was to compare the effect of 12 weeks of HIIT with an equivalent period of MICT or inactivity on appetite regulation in previously inactive, overweight men. There were no statistically significant differences in energy intake at the laboratory test meal or cumulative energy intake after leaving the lab as a result of the intervention period, however, the 95% CI indicated improved appetite regulation after HIIT based on a clinically meaningful decrease in energy intake at the test meal after the HEP compared with LEP in response to HIIT, but not MICT or CON. The tendency for lower energy intake after HEP compared with LEP in response to HIIT suggests improved appetite regulation (taken as, more accurate adjustment of energy intake in response to previous caloric consumption). No significant changes in the perception of appetite were noted as a result of the intervention and the circulating concentrations of glucose, active ghrelin, PP and PYY were not altered across the intervention period. However, insulin was lower following both exercise interventions (fasting – HIIT, postprandial – MICT), but unaltered in CON, while leptin was reduced following HIIT only. Both exercise interventions resulted in a significant increase in aerobic fitness.

Previous research has demonstrated improved appetite regulation in response to a period of aerobic exercise training (23, 24). However, to our knowledge, this is the first study that has compared the effect of different types of exercise training (specifically HIIT with MICT) on appetite regulation. Despite no statistically significant differences in energy intake in response to the intervention, the 95% CI suggests (i.e. lower and upper bound values do not
cross zero; Table 2) that 12 weeks of HIIT significantly improved appetite regulation in response to previous energy intake of differing caloric content, that is; participants ate less at the test meal after HEP compared with LEP (by 516 ± 395 kJ) following HIIT, which was not observed in either the MICT or CON groups. When comparing the HEP condition (pre- vs. post-intervention), a similar decrease in energy intake at the laboratory test meal was observed (by 517 ± 736 kJ) in the HIIT group. After including the self-reported energy intake for the remainder of the test day, MICT appeared to result in more sensitive eating behaviour; that is, cumulative 24 h energy intake after consuming the HEP tended to be lower (by 617 ± 2445 kJ) compared with LEP. While cumulative energy intake following HIIT was not lower after HEP compared with LEP, it should be noted that cumulative energy intake following HIIT was lower after both HEP (by 928 ± 1590kJ) and LEP (by 712 ± 1241kJ) compared with the start of the study. Importantly, considering an energy deficit of 419 kJ and 795 kJ per day has been calculated to prevent weight gain (maintain weight loss) and achieve weight loss respectively (14), the energy deficits presented above may indeed be thought of as clinically meaningful and an important consideration for weight management.

The lack of difference in appetite regulation (HEP vs. LEP) in ad-libitum energy intake at the laboratory test meal after MICT is consistent with previous research of similar duration (23, 24). However, Martins and colleagues (23) reported a significant within group improvement in 24h cumulative energy compensation, which was not observed in the present study. This discrepancy between studies may be explained by differences in the volume of exercise performed. The study of Martins and colleagues (22) involved exercise training 5 times per week compared with 3 times per week in the present study. Additionally, benefits in fasting and postprandial feelings of fullness reported in the study of Guelfi and colleagues (9) following the aerobic exercise intervention were not observed in the present study.

Comment [Kym1]: Include or remove depending on what the others think – keep focus on difference between HEP and LEP?

Comment [Aaron2]: May be interesting information? To show that exercise training resulted in a reduced EI? However, it may be confusing for the reader.

Comment [Aaron3]: To include? or remove? May be important? Explains why HIIT did not result in improvement in appetite regulation? Could be confusing for the reader though.
Surprisingly, the tendency for improved appetite regulation in HIIT was not accompanied by changes in perception of appetite.

With respect to the appetite-related blood variables, we observed attenuated insulin concentration in a fasted state following HIIT and in a post-prandial state following MICT compared with pre-intervention. However, improved insulin sensitivity was only noted following HIIT but not MICT. Given that insulin sensitivity has been reported to have a negative relationship with *ad-libitum* energy intake at a test meal in an overweight population (8, 12), it is possible that the tendency for enhanced appetite regulation following HIIT may be mediated by improved insulin sensitivity. Our findings are in line with those of Matinhomaee and colleagues (25), who also reported that 12 weeks of HIIT improved insulin sensitivity (HOMA-IR index). Importantly, the present study may lend further support to the role of aerobic exercise training as a first-line of defence in the management of insulin resistance, with the observed effect of the HIIT intervention in the present study ($d = 0.512$) not altogether different to that observed with an 8 week intervention with metformin ($d = 0.654$) (15).

The reduction in leptin concentration following HIIT, may be associated with the fat loss (although not significant) observed in the HIIT group (19). In contrast, active ghrelin, PP and PYY were not altered in response to the intervention period. The lack of response of these appetite-related hormones following aerobic exercise training is consistent with the study of Guelfi and colleagues (9), who reported no change in active ghrelin, PP and PYY concentration in sedentary overweight/obese men following 12 weeks of 3 times weekly aerobic exercise training at 70-80% of maximum heart rate. In contrast, Martins and colleagues (22) reported that 12 weeks of aerobic training, 5 times per week at 75% of maximum heart rate resulted in a significant increase in fasting acylated ghrelin.
concentration, together with feelings of hunger in sedentary overweight/obese men and women. Reasons that may explain the discrepancy in outcomes between these studies include differences in the volume of exercise performed and the characteristics of the participants. For instance, the study of Martins and colleagues (22) involved exercise training 5 times per week compared with 3 times per week in the study of Guelfi and coworkers (9) and the present study. Further, given that active ghrelin has been shown to respond differently to aerobic exercise training in men and women (higher active ghrelin concentration in women) (11), the inclusion of women in the study of Martins and colleagues (22) may help explain the difference in findings.

Regardless, this raises the question of the potential mechanisms besides appetite-related blood variables that may have contributed to the tendency for enhanced appetite regulation following HIIT. Firstly, it should be acknowledged that the range of appetite-related peptides measured in this present study is not exhaustive and other appetite related hormones like glucagon-like peptide-1 (GLP-1), cholecystokinin and obestatin also influenced appetite regulation. Furthermore, a series of recent studies have suggested that exercise may have a dampening effect (attenuated neural activity) on the food reward pathways located in the brain which is consistent with reduced general palatability of food, reduced anticipation to eat and reduced food consumption (5-7). Specifically, Crabtree and colleagues (6) demonstrated that high intensity exercise resulted in suppressed neural responses during the viewing of high-calorie foods. Another potential mechanism by which regular exercise training may enhance appetite regulation is via changes to substrate metabolism, in particular, increased fatty acid oxidation which may reduce energy intake via alterations to vagal afferent activity that report satiety signals to appetite centres in the brain (2). Further, changes in psychological approaches to food may result from regular exercise. However, the lack of change in dietary restraint scores observed in the present study suggests a minimal influence
of eating attitudes on appetite regulation. Clearly, further research is required to determine
the mechanisms through which exercise training may affect and improve appetite regulation.

Average HR and RPE over the course of the intervention were found to be higher during
HIIT compared with MICT. Considering the nature of the HIIT protocol (i.e. repeated short
bouts of supramaximal high intensity exercise), this was not unexpected. Despite this, it is
important to note that no differences in physical activity enjoyment were observed between
HIIT and MICT and that enjoyment was greater following both exercise interventions. These
findings are of importance, given that enjoyment of physical activity has been reported to be
a key factor in physical activity performance and exercise adherence (10, 27). The high
attendance rate of study participants in both exercise groups appears to reflect the levels of
enjoyment observed in the present study. Our study also demonstrated that 12 weeks of
aerobic exercise, regardless of exercise protocol resulted in an increase in aerobic fitness.
This is significant given that improvement in aerobic fitness, independent of weight loss has
been associated with improvements with decreased mortality (20).

Finally, while there was a lack of significant alterations in anthropometrical measures (i.e.
body mass and body fat) in response to the intervention period, it should be noted that the
magnitude of change in body fat following HIIT ($d = 0.39$) was comparative with previous
studies that reported statistically significant body fat loss following aerobic exercise
interventions of a similar duration; Martins et al. (23) $d = 0.31$, Guelfi et al. (9) $d = 0.22$. The
lack of statistical significance in the present study may be related to the method of analysis
employed, with the present study comparing differences within (pre vs. post) and between
intervention/control groups, while Martins et al. (23) and Guelfi et al. (9) analysed
differences within (pre vs. post) the intervention groups only.
In summary, we found that HIIT resulted in clinically meaningful improvements in appetite regulation, while an equivalent period of MICT and CON did not. The mechanisms behind this are unclear, with no alterations in the perception of appetite or a number of circulating appetite-related peptides and metabolites in either the fasted state or postprandially, although insulin sensitivity was enhanced in response to HIIT only. Together with previous evidence suggesting the benefits of HIIT for various co-morbidities of obesity (17), findings from the present study may have important implications for current exercise prescription guidelines for individuals exercising for weight loss/maintenance and the management of insulin sensitivity.

Acknowledgements

The hormone assays were carried out with the facilities at the Centre for Microscopy, Characterisation and Analysis, The University of Western Australia that are supported by the funding of the university, state and federal government.

Conflict of interest

The authors declare no conflict of interest.

The results of the present study do not constitute endorsement by the American College of Sports Medicine.


Table 1. Aerobic fitness and body composition before and after 12 weeks of high intensity intermittent exercise training (HIIT; n = 10), moderate intensity continuous exercise training (MICT; n = 10) or no exercise training control (CON; n = 10).

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<th>HIIT</th>
<th>MICT</th>
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<tr>
<td>Peak aerobic capacity - $\dot{V}O_2^{\text{Peak}}$ (ml/kg/min)</td>
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<tr>
<td>Pre</td>
<td>34.8 ± 4.5</td>
<td>34.8 ± 6.2</td>
<td>36.3 ± 5.6</td>
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<td>Post</td>
<td>40.4 ± 4.4 $^a,b$</td>
<td>39.7 ± 6.9 $^a,b$</td>
<td>35.8 ± 5.5</td>
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<td>Body mass (kg)</td>
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<td>85.6 ± 6.4</td>
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<tr>
<td>Post</td>
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<td>85.9 ± 8.5</td>
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<td>27.5 ± 0.9 $^b$</td>
</tr>
<tr>
<td>Body fat percentage (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>32.0 ± 2.9</td>
<td>31.1 ± 5.0</td>
<td>32.2 ± 3.9</td>
</tr>
<tr>
<td>Post</td>
<td>30.9 ± 2.7</td>
<td>30.2 ± 6.5</td>
<td>32.5 ± 3.9</td>
</tr>
</tbody>
</table>

Pre and post values presented as mean ± SD and Cohen’s $d$ effect size; $^a$Indicates significant difference from pre-intervention ($p \leq 0.050$). $^b$Indicates moderate-large effect size from pre-intervention.
Table 2. Difference in *ad-libitum* energy intake from a laboratory test meal and cumulative 24 h energy intake (kJ) after a high energy preload (HEP) and low energy preload (LEP), before and after 12 weeks of high intensity intermittent exercise training (HIIT), moderate intensity continuous exercise training (MICT) or no exercise training (CON; n = 10 in each group).

<table>
<thead>
<tr>
<th>Preload</th>
<th>HIIT</th>
<th>MICT</th>
<th>CON</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
</tr>
<tr>
<td>Δ energy intake at test meal (HEP vs. LEP intervention)</td>
<td>43 ± 585 [-320, 406]</td>
<td>516 ± 395 [271, 762]</td>
<td>68 ± 677 [-351, 488]</td>
</tr>
<tr>
<td>Δ 24 h energy intake (HEP vs. LEP intervention)</td>
<td>-402 ± 1597 [-1392, 588]</td>
<td>-649 ± 2103 [-1953, 654]</td>
<td>204 ± 1054 [-449, 857]</td>
</tr>
<tr>
<td>Δ energy intake at test meal (pre vs. post-intervention)</td>
<td>517 ± 736 [61, 973]</td>
<td>199 ± 1043 [-447, 845]</td>
<td>-223 ± 628 [-612, 166]</td>
</tr>
<tr>
<td>Δ 24 h energy intake (pre vs. post-intervention)</td>
<td>928 ± 1590 [-58, 1913]</td>
<td>758 ± 1917 [-430, 1946]</td>
<td>-199 ± 648 [-601, 203]</td>
</tr>
</tbody>
</table>

Values presented as mean (x̅) and 95% confidence interval (CI) for pre-intervention energy intake subtract post-intervention energy intake [lower bound, upper bound]. Where the 95% CI does not cross zero, the value is bolded.
Figure 1. Mean (± SE) *ad-libitum* energy intake at laboratory test-meal following a high energy preload (HEP) and low energy preload (LEP) before (pre-intervention) and after (post-intervention) 12 weeks of high intensity intermittent exercise training (HIIT), moderate intensity continuous exercise training (MICT) or no exercise training (CON) (*n* = 10 in each group).
Figure 2. Mean (± SE) cumulative 24 h energy intake following a high energy preload (HEP) and low energy preload (LEP) before (pre-intervention) and after (post-intervention) 12 weeks of high intensity intermittent exercise training (HIIT), moderate intensity continuous exercise training (MICT) or no exercise training (CON) \((n = 10\) in each group).
Figure 3.

Mean (± SE) concentrations of (A) insulin, (B) leptin, (C) active ghrelin, (D) PP, (E) PYY, (F) glucose in the fasted state (time 0 min) and in response to caloric consumption (indicated by upward arrow↑) before (represented by ●) and after (represented by ○) 12 weeks of high intensity intermittent exercise training (HIIT), moderate intensity continuous exercise training (MICT) or no exercise training control (CON) (n = 10 in each group).
Significantly different from pre-intervention. * Significant interaction effect of pre- vs. post-intervention, test session time (0, 35, 65 min) and condition (HIIT, MICT and CON). † Significant main effect of test session time-point (0, 35, 65 min) - different from pre-intervention. \( p \leq 0.05 \).