Effects of a Fat-sugar Supplemented Diet, with and Without Exercise Training, on Body Fat Mass and Selected Cardiometabolic Risk Markers in Overweight and Obese, Sedentary Males

by

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ABSTRACT

The winter holiday period has been highlighted as a major risk period for weight gain due to excess caloric intake in the form of fat and sugar. Furthermore, diets high in fat and sugar have been implicated in the pathogenesis of diabetes and cardiovascular disease. Exercise aids in the prevention of weight/fat gain, and prevents deleterious changes in cardiometabolic function. The objective of this study was to examine the effects of a fat-sugar supplemented diet, with and without two different exercise training protocols, on body composition, glycemic control and other markers of cardiovascular disease in an at-risk population of overweight and obese males. Twenty-seven, healthy overweight/obese (BMI >25 kg/m^2) males were fed 2 donuts per day, 6 days/week, for four weeks, while maintaining their current diet. In addition, all subjects were randomized to one of the following conditions: sedentary control, 1,000 kcal/week moderate-intensity continuous training (MICT) (50% of peak oxygen consumption), or 1,000 kcal/week high-intensity interval training (HIIT) (90-95% of peak heart rate). Supervised exercise training was performed 4 days/week on a cycle ergometer. Changes in body weight and composition, endothelial function, arterial stiffness, glycemic control, blood lipids and cardiorespiratory fitness (CRF) were assessed before and after the intervention. Body weight, lean mass and visceral fat increased significantly in HIIT ($p<0.05$) and were unchanged in MICT. There was a trend for a significant increase in body weight ($p=0.07$) and lean mass ($p=0.11$) in control. Glycemic control during the 2-h OGTT improved significantly in MICT and control, with no change in HIIT. Hepatic insulin resistance index (IRI) and 30-min insulin during the OGTT improved significantly after MICT and worsened following control ($p=0.03$), while HIIT was

unchanged. CRF increased significantly in both HIIT and MICT, with no change in control ($p<0.001$). There were no significant changes in other markers of cardiovascular disease. The addition of a fat-sugar supplement (~14,500 kcal) over a 4-week period was not sufficient to induce deleterious changes in body composition and cardiometabolic health in overweight/obese young males. Exercise training did not afford overweight/obese males additional health benefits, with the exception of improvements in fitness and hepatic IRI.

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CHAPTER 1

INTRODUCTION

According to CDC estimates in 2012, nearly 70% of US adults are overweight or obese (Ogden, Carroll, Kit, & Flegal, 2014). It is estimated that the average U.S. adult gains ~0.5-1.0 kg body weight annually (Flegal & Troiano, 2000; Hill, Wyatt, Reed, & Peters, 2003; Truesdale et al., 2006). The winter holiday period has been highlighted as a major risk period for weight gain due to excess caloric intake and decreased physical activity (Haines, Hama, Guilkey, & Popkin, 2003; Ma et al., 2006; Roberts & Mayer, 2000). Studies indicate that individuals typically gain 0.5-0.8 kg of body weight during this holiday period (mid-November through New Year's Day) (Hull, Hester, & Fields, 2006; Stevenson, Krishnan, Stoner, Goktas, & Cooper, 2013; Yanovski et al., 2000) and this weight gain does not appear to be reversed in the ensuing months (Yanovski et al., 2000), suggesting that the holiday period contributes substantially to annual weight gain and obesity. Evidence also indicates that the majority of weight gained during the holiday period is in the form of body fat (Hull, Radley, Dinger, & Fields, 2006; Stevenson et al., 2013), which increases risk of mortality and morbidity (particularly if it occurs as visceral or intrahepatic fat) (Fabbrini et al., 2009; Kissebah, 1996; Reaven, Abbasi, & McLaughlin, 2004).

One of the first studies to quantify holiday weight gain was conducted by Yanovski and colleagues (2000) in a convenience sample of 195 adults at the National Institute of Health (NIH). Subjects were told that the study was a general health assessment and vital signs were taken to mask the true intent of the study. Body weight was measured at 3 time points: Pre-holiday (Sept/Oct to mid-Nov), holiday (mid-Nov to

early January) and post-holiday (early to mid-Jan to late Feb or early March). The researchers found that body weight increased significantly during the holiday period (+0.37 kg, $p<0.001$) but not during the pre-holiday (+0.18 kg), post-holiday periods (-0.07 kg). In the 165 subjects who were weighed 1 year after the study, 65% of the annual weight gain observed during the 1-year observation period was gained during the holiday period alone. Similarly, Hull and colleagues (2006) reported a 0.5 kg weight gain during the Thanksgiving holiday break (~13 days) in 94 college students at the University of Oklahoma. Stevenson et al. (2013) assessed changes in body composition and body weight in 148 adults in mid-November and again in early January. The results demonstrated a significant increase in body weight (+0.78 kg, $p<0.001$) and percent body fat (+0.5%, $p=0.007$) during the winter holidays.

Closer examination of these observational studies reveals that overweight and obese individuals are more likely to gain significant body weight than normal weight individuals during the winter holidays (Hull, Hester et al., 2006; Stevenson et al., 2013; Yanovski et al., 2000). High self-report physical activity levels have been shown to prevent holiday weight gain in one study (Yanovski et al., 2000) but failed to prevent holiday weight gain in another study (Stevenson et al., 2013). However, self-report physical activity levels have been shown to be inaccurate and unreliable (van Poppel, Chinapaw, Mokkink, van Mechelen, & Terwee, 2010). Cook and colleagues (2012) showed high baseline total energy expenditure (assessed by Doubly Labeled Water) were insufficient to prevent holiday weight gain in middle-aged adults (Cook, Subar, Troiano, & Schoeller, 2012). However, the ability of objectively measured increases in physical activity to prevent weight gain during the winter holiday period is unknown.

Exercise intensity is independently related to obesity prevalence and weight gain over time (Bailey, Tucker, Peterson, & LeCheminant, 2007; DiPietro, Kohl, Barlow, & Blair, 1998; DiPietro, Williamson, Caspersen, & Eaker, 1993; French et al., 1994). High-intensity interval training (HIIT) is a popular, time-efficient exercise modality that typically consists of brief periods (30 seconds to 4 min) of high-intensity exercise (90-95% of peak heart rate) interspersed with periods of low-intensity active recovery. Two recent reviews concluded that HIIT is as effective or perhaps superior to traditional, continuous exercise (walking or jogging) for promoting fat loss and aiding weight maintenance (Boutcher, 2011; Kessler, Sisson, & Short, 2012). Furthermore, HIIT may also be superior for reducing harmful visceral fat (Tjonna et al., 2008; Trapp, Chisholm, Freund, & Boutcher, 2008; Tremblay, Simoneau, & Bouchard, 1994) and other risk factors associated with cardiovascular disease and diabetes (Kessler et al., 2012; Weston, Wisloff, & Coombes, 2014). Recently, Black (2013) demonstrated that 4 days a week of exercise training (2 days of HIIT and 2 days of MICT) prevented weight and fat gain during 3 weeks of fat-sugar supplemented diet (+12,000 kcal) in young, healthy males. In contrast, those in the sedentary control group gained 1.7 kg of body weight (1.4 kg of fat) during the intervention. Further studies are needed to assess whether HIIT or MICT is superior for the prevention of weight gain during periods of high caloric intake.

Physical inactivity and a high-fat, high calorie diet do not only play a pivotal role in weight gain and obesity but also in the development of type 2 diabetes (Booth, Laye, Lees, Rector, & Thyfault, 2008; Zimmet, Alberti, & Shaw, 2001). Brief periods of overfeeding have been shown to adversely affect insulin sensitivity (Adochio, Leitner, Gray, Draznin, & Cornier, 2009; Anderson et al., 2015; Brons et al., 2009). Similarly, as

little as a few days of physical inactivity reduces insulin sensitivity in healthy adults (Hamburg et al., 2007; Heath et al., 1983; Thyfault & Krogh-Madsen, 2011). Furthermore, a combination of reduced physical activity and overfeeding decreases insulin sensitivity and impairs glucose metabolism within a matter of days (Hagobian & Braun, 2006; Knudsen et al., 2012; Krogh-Madsen et al., 2014). These findings suggest that short periods of high caloric intake and physical inactivity may play an integral role in the development of diabetes and cardiovascular disease.

Atherosclerotic cardiovascular disease (CVD) is the number one cause of death in the United States and the developed world (Lloyd-Jones et al., 2009). Between 2010 and 2030, total direct medical costs of CVD are projected to triple, from $273 billion to $818 billion (Heidenreich et al., 2011). High caloric intake (particularly in the form of fat) has been shown to increase the risk of cardiovascular disease via increases in triglycerides (Ortega, Fernandez-Elias, Hamouti, & Mora-Rodriguez, 2013), cholesterol (Stamler, Wentworth, & Neaton, 1986), blood pressure (Jakulj et al., 2007; Stamler et al., 1986; Straznicky, Louis, McGrade, & Howes, 1993), arterial stiffness (Orr, Gentile, Davy, & Davy, 2008; Rider et al., 2012) and endothelial dysfunction (Vogel, Corretti, & Plotnick, 1997). Similarly, physical inactivity has been implicated as a major cause of endothelial dysfunction and cardiovascular disease (Laufs et al., 2005). Since the winter holiday period is characterized by excessive caloric intake and physical inactivity, treatment strategies directed towards prevention of atherosclerosis and insulin resistance during this time period are paramount for reduction of obesity, cardiovascular disease and diabetes.

Maintaining or increasing normal physical activity during times of overfeeding has also been shown to eliminate the deleterious cardiometabolic effects typically

associated with high-caloric intake (Krogh-Madsen et al., 2014; Walhin, Richardson, Betts, & Thompson, 2013). Krogh-Madsen and colleagues (2014) demonstrated that maintaining regular physical activity (>10,000 steps/day) during 14 days of overfeeding (+2,000 kcal/day) prevented increases in visceral fat, insulin resistance, worsened glycemic control, decreased cardiorespiratory fitness and hyperlipidemia which was exhibited by the sedentary control group (<1,500 steps/day). Walhin et al. (2013) showed that daily vigorous exercise training (45 min of treadmill running at 70% of maximal oxygen uptake) during 7 days of overfeeding (+50% daily energy intake) maintained insulin sensitivity and blood lipids. In contrast, the sedentary control group (<4,000 steps/day) demonstrated a 2-fold increase in 2-h insulin iAUC during the oral glucose tolerance test (OGTT) as well as deleterious alterations in the expression of several key genes associated with insulin action in adipose tissue. This demonstrates that exercise training may counteract deleterious cardiometabolic effects typically associated with excess caloric intake and physical inactivity. However, it should be noted that the subjects in these studies were young, lean (BMI < 25 kg/m^2) and recreationally active (VO_{2max} > 55 ml/kg/min) (Krogh-Madsen et al., 2014; Walhin et al., 2013). In addition, while these study designs may be suitable for elucidating mechanisms associated with periods of excess caloric intake and physical inactivity, the likelihood of individuals increasing daily intake by 1,500 to 2,000 kcal and reducing step counts to less than 1,500 steps is unlikely over the course of several weeks.

No studies have examined the impact of exercise intensity, particularly high-intensity interval exercise, on holiday weight gain or cardiometabolic health during short-term overfeeding in an at-risk population of sedentary overweight and obese males. The

proposed research is designed to fill this research gap. The proposed research is especially applicable to overweight and obese adults because previous studies indicate that they are most at-risk for weight gain during the holiday periods (Stevenson et al., 2013; Yanovski et al., 2000).

The purpose of the current study is to assess the effects of a fat-sugar supplemented diet, with and without two different exercise training protocols, on body composition, glycemic control, cardiorespiratory fitness, vascular function and other blood markers of cardiovascular risk in an at-risk population of overweight and obese, sedentary males.

Specific aims and hypotheses

The primary specific aim was to test the efficacy of moderate-intensity continuous training (MICT) and high-intensity interval training (HIIT) exercise on preventing body weight and fat mass gain during a 4-week period of fat-sugar supplemental feeding in overweight and obese, sedentary males. I hypothesized that the control group would result in a significant weight and fat mass gain in comparison to both exercise groups. I also hypothesized that the HIIT group would result in significantly less weight and fat mass gain than the MICT group.

A secondary specific aim was to determine the effectiveness of MICT and HIIT exercise to prevent deleterious cardiometabolic effects such as endothelial dysfunction, arterial stiffness, insulin resistance, impaired glycemic control and reduction in cardiorespiratory fitness associated with 4-weeks of fat-sugar supplemental feeding. I hypothesized that the control group would exhibit significant adverse changes in markers of cardiometabolic health in comparison to both exercise groups. I also hypothesized that the HIIT group would have better preservation of markers of cardiometabolic health compared to MICT.

CHAPTER 2

REVIEW OF LITERATURE

Fat-Sugar Supplemented Diets, Weight Gain and Cardiovascular Disease

The winter holiday period is a time when cultural and social influences combine to create a high risk environment conducive to weight gain (Hull, Radley et al., 2006). Longer eating durations, easy access to food, eating in the presence of others, and increased portion sizes (Wansink, 2004) are all present and contribute to overeating during the holidays. Furthermore, foods typically consumed during the winter holidays are typically high in fat and sugar, creating an ideal macronutrient profile for body weight and fat gain.

Overfeeding humans with a mixed diet of fat and sugar induces a positive energy balance that mainly results in fat gain (Ernersson, Nystrom, & Lindstrom, 2010; Knudsen et al., 2012; Ravussin et al., 1985). A seminal study by Ravussin and colleagues (1985) revealed the changes in carbohydrate and fat balance during overfeeding on a mixed diet in young men. After 13 days on a weight maintenance diet, the young men were overfed (+60% typical intake) for 9 days with a mixed diet of fat and carbohydrate. Over the 9 days of overfeeding on the mixed diet, carbohydrate oxidation increased until carbohydrate balance was achieved with a minor contribution of ingested carbohydrate going towards carbohydrate storage. In contrast, fat utilization decreased and fat storage increased to reflect a large portion of the lipid intake. These findings demonstrate that during overfeeding with a mixed diet, carbohydrate balance tends towards zero whereas fat balance mainly reflects the change in energy balance mainly in the form of fat gain (Jequier, 1993). Furthermore, subsequent studies (Acheson et al., 1988; Horton et al.,

1995; Schutz, Flatt, & Jequier, 1989) showed that humans increase carbohydrate oxidation and total energy expenditure when they ingest excess dietary carbohydrate (Acheson et al., 1988; Horton et al., 1995), but fail to increase fat oxidation or total energy expenditure when they overconsume dietary fat (Horton et al., 1995; Schutz et al., 1989). These findings suggest that excess energy as fat is stored more efficiently than carbohydrate and leads to greater fat accumulation during periods of overfeeding.

Bobbioni-Harsch et al. (1997) examined differences in energy balance and substrate partitioning after three isocaloric loads of differing macronutrient compositions in 10 lean, healthy adults (5 men, 5 women). On 3 separate visits subjects consumed a meal (636 kcal) consisting of either: 100% glucose, 95% fat, or a mixed meal (50% fat, 50% glucose). Respiratory quotient (RQ) increased significantly after consuming the 100% glucose meal and after the mixed meal indicating an increase in glucose oxidation and decrease in fat oxidation in these conditions, but RQ remained the same after consuming the high fat meal with no increase in glucose oxidation and a slight elevation in fat oxidation. These findings reveal a prioritization towards carbohydrate oxidation (at the expense of fat oxidation) during consumption of a mixed meal (Bobbioni-Harsch et al., 1997). Thus overfeeding with a fat-sugar supplemented diet typically yields rapid weight gain through the prioritization of glucose oxidation and storage of fat as previously demonstrated (Ravussin et al., 1985). Thus it appears that macronutrient composition of energy intake may play an important role in the development of weight gain.

Short-term increases in energy intake and alterations in macronutrient composition appear to play a pivotal role in weight gain and obesity (Horton et al., 1995;

Jequier, 1993). However, studies show that slight alterations in physical activity during periods of high caloric intake can also be a significant contributor to changes in energy balance in the body (Ernersson et al., 2010; Stubbs et al., 2004). Stubbs and colleagues (2004) assessed the effects of decreased physical activity on appetite, energy intake and energy balance in 6 young, lean men over 7 days of ad-libitum feeding. All subjects underwent 2 separate conditions on different days: a sedentary condition at 1.4 times resting metabolic rate (RMR), and a moderately active condition at 1.8 times RMR. All subjects resided in a whole body indirect calorimeter for the 7-day duration of each condition to assess energy expenditure. During each condition, subjects were given access to an ad-libitum mixed diet (47% fat, 40% carbohydrate, 13% protein) and energy intake, meal frequency, hunger and appetite were all continuously tracked. As anticipated, energy expenditure during the moderately active condition (1.8 times RMR) was significantly higher than the sedentary condition (1.4 times RMR). However, energy intake, hunger and appetite were not different between the two conditions. This yielded a greater cumulative energy balance and weight gain in the sedentary group compared to the active group. These results show that a decrease in physical activity does not create a compensatory reduction in short-term energy intake and yield greater increases in weight gain during periods of high caloric intake.

To assess the effects of short-term overfeeding and reduced physical activity (PA) on long-term weight gain, Ernersson et al. (2010) overfed young normal weight adults with fast food for 4 weeks and assessed changes in body weight and composition before and after the intervention, as well as 12 months post-intervention. Eighteen subjects (12 men and 6 women, mean age = 26 years) increased their energy intake with fast food by

70% (+1,495 kcal/day) and reduced PA (<5,000 steps a day) for 4 weeks. An age and gender matched control group was recruited and asked not to change their diet or PA levels during the 4-week intervention. Body composition changes were measured by DXA at baseline, after the 4-week intervention and 12 months post-intervention. The overfeeding group increased body weight significantly at 4 weeks (+6.4 kg) with the DXA showing increases in both fat and fat-free mass. Twelve months later, body weight was significantly reduced (−4.9 kg) but still significantly elevated relative to baseline body weight (+1.5 kg) in the overfeeding group. Furthermore, DXA measurements revealed that almost all of the increased body weight at 12 months was due to changes in fat mass (+1.4 kg). A follow-up assessment of body weight at 2.5 years post-intervention showed a significant increase of 3.1 kg relative to baseline in the overfeeding group, while there was no change in body weight (+0.1 kg) among controls.

A similar study with a shorter duration was conducted by Knudsen et al. (2012) and examined the effects of 14 days of step reduction combined with overfeeding on changes in insulin sensitivity and body composition in healthy young men. Nine men (mean age = 24 years, BMI 21.6 kg/m^2) who met the public health recommendations of 10,000 steps/day, underwent 14 days of step reduction (1,500 steps/day) and overfeeding (+50% caloric intake) to reach a daily positive energy balance of ~2,000 kcal/day. The overfeeding protocol consisted of a daily snack package (1,500 kcal) containing a variety of high fat, high sugar foods such nuts, cakes, chocolates, potato chips and sodas. Body composition (DXA, MRI) and insulin sensitivity (OGTT and hyperinsulinemic euglycemic clamp) were assessed at baseline, day 3, 7 and 14 of the intervention, with follow-up tests at day 30. Insulin sensitivity (assessed by Matsuda Index) decreased

significantly at day 3 and 7 compared to baseline. Furthermore, insulin levels were significantly elevated during the OGTT at day 7 and 14 and glucose infusion rates declined by 44% at day 14 during the hyperinsulinemic-euglycemic clamp relative to baseline values. Body weight increased significantly at day 7 (+1.7 kg) and 14 (+1.8kg), with the majority of weight gained in the form of fat (+1.0 kg at day 7 and 1.5 kg at day 14). These findings reveal that a decrement in insulin sensitivity preceded adverse changes in body composition during overfeeding and physical inactivity. Interestingly, insulin sensitivity was completely restored two weeks after resumption of normal physical activity, whereas increases in body fat remained.

These studies reveal that short periods of high fat-sugar supplemented overfeeding coupled with reductions in physical activity (such as observed during the winter holidays) may contribute significantly to annual weight gain and deleterious cardiometabolic changes responsible for chronic disease.

Holiday Weight Gain and the Impact of Physical Activity

It is commonly asserted that most Americans gain 5-10 pounds (2.3 to 4.5 kg) of body weight over the winter holiday period between Thanksgiving and New Year's day (Rosenthal, Genhart, Jacobsen, Skwerer, & Wehr, 1987; Thompson, Stinson, Fernandez, Fine, & Isaacs, 1988). However, these numbers reflect self-report or people's perceived weight gain during the winter holidays making them unreliable and potentially inaccurate.

Yanovski et al. (2000) sought to objectively quantify holiday weight gain by assessing changes in body weight in a convenience sample of 195 adults. The subjects (mean age = 39 years, 51% female, 67% Caucasian) were weighed on four occasions at

intervals of 6 to 8 weeks, so that change in body weight was determined for three periods: Pre-holiday (Sept/Oct to mid-Nov), holiday (mid-Nov to early January) and post-holiday (early to mid-Jan to late Feb or early March). A final measurement of body weight was also take in 165 of the subjects 1 year after the pre-holiday testing. Data on other vital signs and self-reported health measures were collected in order to mask that body weight was the main outcome of interest. The researchers found that body weight increased significantly during the holiday period (+0.37 kg, $p<0.001$) but not during the pre-holiday (+0.18 kg) and post-holiday periods (-0.07 kg). The average net weight gain during the intervention period was +0.48 kg ($p=0.003$). Furthermore, when subjects were categorized as normal weight, overweight and obese according to their BMI, overweight and obese subjects were more likely to experience major weight gain ($\geq$ 2.3 kg) during the holiday period. In the 165 subjects who returned for 1-year follow-up, 65% of the annual weight gain observed during the 1-year observation period was gained during the holiday period alone. Self-report data gathered from questionnaires during the intervention revealed that only changes in physical activity and hunger were predictive of holiday weight gain during the intervention.

To examine whether individuals with high-energy expenditures were less susceptible to seasonal weight gain, Cook and colleagues (2012) tested whether holiday weight gain was reduced in participants with high baseline total energy expenditure (TEE). Changes in body weight over a 90-day period were assessed between mid-September 1999 and Mid-January 2000 in 443 men and women (40-69 years old). Baseline total energy expenditure (TEE) was measured using the gold standard doubly labeled water. The researchers found no correlation between TEE or physical activity

levels at baseline and change in body weight during the winter holidays. These findings suggest that a high pre-holiday TEE does not appear to protect against seasonal weight gain. However, the authors of this study acknowledge that it is unknown whether higher TEE (such as those seen with exercise training interventions) would be protective against holiday weight gain.

To better quantify the effects of physical activity on preventing holiday weight gain, Stevenson et al. (2013) assessed changes in body composition, blood pressure and the impact of regular exercise on these parameters during the holiday season. A total of 148 adults (mean age = 34, mean BMI = 25.1 kg/m^2, 100 females, 80% Caucasian) were assessed for anthropometry, blood pressure and self-reported physical activity in mid-November (visit 1) and again in early January (visit 2). Similar to the Yanovski et al. (2000) study, the subjects were masked to the true outcomes of the study by telling the subjects that the study was about 'short-term changes in health parameters'. The subjects demonstrated a significant increase in body weight (+0.78 kg, $p<0.001$), percent body fat (+0.5%, $p=0.007$), systolic blood pressure (+2.3 mmHg, $p=0.04$) and diastolic blood pressure (+1.8 mmHg, $p=0.03$). Weight gain during the holidays was extremely heterogeneous with a range of -2.3 to 6.3 kg. Furthermore, obese subjects showed a greater increase in body fat ($p<0.05$) and a trend towards a greater increase in systolic BP ($p=0.06$) compared with normal and overweight individuals. It should be noted that percent body fat changes were assessed by bioelectrical impedance analysis. This method is not a criterion measure for tracking changes in body composition and can have a standard error estimate of 3-4% even when hydration and exercise are carefully controlled (Eckerson, Stout, Housh, & Johnson, 1996; J. G. Wang et al., 2013). Self-

reported physical activity (4.8 hours per week) did not protect against holiday weight gain and was not a significant predictor of changes in body weight or body fat (Stevenson et al., 2013). However, self-reported physical activity data relies heavily on the participant's memory and accuracy of reporting which are both prone to high estimation error (van Poppel et al., 2010). Self-report physical activity and physical activity questionnaires have been shown to overestimate physical activity levels by 36 to 173 percent compared to objective measures of physical activity (Lee, Macfarlane, Lam, & Stewart, 2011).

Another study conducted by Hull and colleagues (2006) at the University of Oklahoma examined weight gain during the Thanksgiving holiday only (~13 days). Body weight changes were measured in 94 college students (mean age = 23, mean BMI = 24 kg/m^2, 50 females). The researchers found a significant increase in body weight (+0.5 kg) despite a much shorter holiday duration compared to previous studies assessing changes in body weight during the winter holidays (Stevenson et al., 2013; Yanovski et al., 2000). Also, males (+0.6 kg) gained more body weight than females (+0.4 kg) during the Thanksgiving period. Similar to previous findings (Stevenson et al., 2013; Yanovski et al., 2000), overweight or obese (BMI $\geq$ 25 kg/m^2) subjects gained significantly more body weight (+1.0 kg) than normal weight individuals (+0.2 kg) during the Thanksgiving period.

Taken together, the studies quantifying holiday weight reveal that most Americans gain between 0.5 and 0.8 kg during the winter holiday period (Cook et al., 2012; Hull, Hester et al., 2006; Stevenson et al., 2013; Yanovski et al., 2000). This suggests that the holiday period may play a major role (50-80%) in contributing to annual

weight gain among US adults. Furthermore, overweight and obese individuals (who encompass greater than two-thirds of the adult US population) are more susceptible to body weight and fat gain during the seasonal period (Hull, Hester et al., 2006; Stevenson et al., 2013; Yanovski et al., 2000). Studies assessing the impact of physical activity levels on holiday weight gain have yielded mixed results (Stevenson et al., 2013; Yanovski et al., 2000) possibly due to poor methodology for tracking physical activity (self-report data). Although high baseline TEE levels (assessed with doubly labeled water) do not seem to protect against holiday weight (Cook et al., 2012), it is unclear if exercise interventions during the holiday period may be protective against weight gain and deleterious cardiometabolic outcomes.

Protective Effects of Physical Activity During Energy Surplus

To my knowledge no studies have assessed the efficacy of changes in physical activity to alter weight gain and deleterious cardiometabolic effects during the winter holiday period. However, studies of short-term overfeeding and altered physical activity levels may provide us with a good simulation of the body composition and metabolic changes that typically occur during the winter holiday period.

Krogh-Madsen and colleagues (2014) examined whether maintaining levels of physical activity (10,000 steps/day) can prevent deleterious body composition and metabolic effects during a period of high-caloric intake. Twenty young, normal weight males (mean age = 22 years; BMI = 22 kg/m; VO_{2max} ~60 ml/kg/min) were randomized to either 10,000 steps/day plus 2,000 additional kcal/day or 1,500 steps/day plus 1,500 additional kcal/day for 14 days. Groups were matched for energy surplus. The overfeeding protocol consisted of a daily snack package (1,500 kcal) containing a variety

of high fat, high sugar foods such nuts, cakes, chocolates, potato chips and sodas. Steps, total energy expenditure, dietary records, cardiorespiratory fitness, body composition (DXA and MRI), continuous glucose monitoring (CGM) and OGTT with stable isotopes were administered before and after the intervention. Both groups gained significant body weight but the inactive group (+1.6 kg) gained more than the active group (1.0 kg). However, the inactive group gained significantly more total, android and visceral fat compared to the active group. Furthermore, the inactive group also experienced worse glycemic control assessed by CGM and increased endogenous glucose production and decreased hepatic insulin extraction assessed by OGTT tracers. The active group maintained cardiorespiratory fitness and blood lipids while those in the inactive group experienced a decrement in VO2max and an increase in total and LDL cholesterol. These findings reveal that maintenance of normal daily physical activity levels during periods of overfeeding can prevent increases in total and visceral body fat as well as declines in metabolic health in young healthy males.

Walhin et al. (2013) examined whether daily exercise training could prevent impaired metabolic function associated with short-term overfeeding. Twenty-six young active, normal weight males (mean age = 25 years; BMI = 23.8 kg/m^2; VO_{2max} = ~57 ml/kg/min) were randomized to either physical inactivity (<4,000 steps/day) plus overfeeding (+50% kcal) or 45 min of vigorous treadmill running (70% of VO_{2max}) plus overfeeding (+75% kcal) for 7 days. Groups were matched for energy surplus. Fasted blood samples and abdominal subcutaneous fat biopsies were obtained before and after the intervention. In addition, all subjects underwent a 2-hour oral glucose tolerance test (OGTT) at baseline and follow-up with blood samples taken every 15 minutes to assess

glucose, insulin and C-peptide. Step count targets were tracked and confirmed with pedometers during the intervention. After 7 days of overfeeding, body weight and lean mass increased significantly in both sedentary (+2.7 kg body weight; +2.6 kg lean mass) and exercise intervention (+1.6kg body weight; +1.0 kg lean mass) groups. However, these increases were significantly lower in the exercise group. The glycemic response following the OGTT was unchanged following the intervention in both groups. However, there was a significant 2-fold increase in 2-h insulin iAUC and C-peptide in the sedentary group, while these measures remained unchanged in the exercise group. Furthermore, overfeeding yielded deleterious alterations in the expression of several key genes involved with insulin action and these changes were only present in the sedentary group. These findings suggest that daily vigorous-intensity exercise may prevent the reduction in insulin sensitivity, hyperinsulinemia and altered gene expression of several key genes within adipose tissue that typically accompany short-term overfeeding and reduction in physical activity.

In a similar study, Black (2013) completed a pilot trial to establish the feasibility of vigorous-intensity exercise training for preventing weight gain during a 3-week period of overfeeding. Young, normal weight adult males (n=19) consumed 12 donuts per week (~4,000 kcals) in addition to their normal diet and were randomized to one of two groups: control (12 donuts per week, no exercise) or exercise training (12 donuts per week + 30 min, 4 days per week of aerobic exercise). The aerobic exercise consisted of two sessions of moderate-intensity, continuous (MOD) and two sessions of HIIT per week (120 min total exercise time/week) either cycling on a stationary exercise bike or running on a treadmill. The results showed a significant difference between groups for body weight

and fat mass ($p<0.05$). The control group gained 1.7 kg of body weight (1.4 kg fat), while the intervention group showed little to no gain in body weight or fat even though the difference between energy expended (~4,500 kcal) and energy consumed (~12,000 kcal) yielded an estimated energy surplus of ~7,200 kcal. The researchers also witnessed a significant increase in cardiorespiratory fitness and strong trends towards improvements of insulin sensitivity (measured by HOMA-IR) in the exercise group only. However, this study used a young, healthy active population which may not be as at-risk to the seasonal effects of overfeeding and physical inactivity as an overweight/obese sedentary population (Hull, Radley et al., 2006; Knudsen et al., 2012; Stevenson et al., 2013; Yanovski et al., 2000). Furthermore, since both MOD and HIIT were included as part of the exercise group, it is uncertain which exercise intensity and modality is more effective for eliciting these protective effects.

Exercise Intensity, Energy Balance and Fat Loss

Cross-sectional and prospective studies have shown that exercise intensity is independently related to obesity prevalence and weight gain over time (Bailey et al., 2007; DiPietro et al., 1998; DiPietro et al., 1993; French et al., 1994). Recent studies that have included high-intensity interval training (HIIT) as part of a lifestyle intervention program, show that HIIT is as effective or perhaps superior to traditional, continuous exercise (walking or jogging) for promoting fat loss and aiding with weight maintenance (Boutcher, 2011; Hunter, Weinsier, Bamman, & Larson, 1998; Tjonna et al., 2008; Trapp et al., 2008). Furthermore, HIIT is more time-efficient, enjoyable and successful at reducing harmful visceral fat than moderate-intensity exercise (Tjonna et al., 2008; Trapp, Chisholm, & Boutcher, 2007; Tremblay et al., 1994).

Possible mechanisms underlying the HIIT-induced fat and weight loss include: increased resting energy expenditure (REE) (Hunter, Byrne, Gower, Sirikul, & Hills, 2006; Maehlum, Grandmontagne, Newsholme, & Sejersted, 1986; Treuth, Hunter, & Williams, 1996) due in part to increases in sympathetic tone (Hunter et al., 2006), increased exercise (Talanian, Galloway, Heigenhauser, Bonen, & Spriet, 2007) and post-exercise fat oxidation (Tremblay et al., 1994), as well as increased excess post-exercise oxygen consumption (Borsheim & Bahr, 2003). Furthermore, the inefficient nature of HIIT creates increases in energy expenditure during exercise compared to lower-intensity exercise (Hunter et al., 1998). Talanian et al. (2007) showed that just seven bouts of HIIT over a 2-week period increased whole body fat oxidation by 36% by significantly upregulating muscle β-hydroxyacyl coenzyme A dehydrogenase, a key rate-limiting enzyme in fat oxidation. Total muscle plasma membrane fatty acid binding protein content also increased significantly. These adaptations demonstrate an increased skeletal muscle capacity for fatty acid oxidation.

Excess post-exercise oxygen consumption (EPOC) is the increased oxygen utilization over rest that can extend for hours after exercise (Gaesser & Brooks, 1984), and is significantly affected by exercise intensity (Borsheim & Bahr, 2003). HIIT has been shown to result in a significantly greater increase in EPOC several hours post-exercise compared with continuous, endurance exercise (Bahr, Gronnerod, & Sejersted, 1992; Laforgia, Withers, Shipp, & Gore, 1997; Larsen, Welde, Martins, & Tjonna, 2014). However, two of these studies (Bahr et al., 1992; Laforgia et al., 1997) included supramaximal interval protocols (>105% VO_{2max}) with long durations (1-2 minutes) in recreationally active young adults, which may not be a suitable exercise training protocol

for the general population. Two recent studies (Skelly et al., 2014; Tucker, Angadi, & Gaesser, 2016) investigating EPOC with more practical models of HIIT (10x1 HIIT or 4x4 HIIT protocols at 90-95% HR_{max}) showed that HIIT did not induce a greater EPOC than MICT in the hours directly following exercise. These findings suggest that it is unlikely that the greater fat loss observed in HIIT training studies (Macpherson, Hazell, Olver, Paterson, & Lemon, 2011; Trapp et al., 2008; Tremblay et al., 1994) are attributable to greater EPOC.

HIIT is a potent, time-efficient exercise modality for promoting weight and fat loss. However, the ability of HIIT or MICT to prevent weight and fat gain that typically accompanies overfeeding or high caloric intake is unknown.

Exercise Intensity and Cardiometabolic Health

Overfeeding and physical inactivity induce insulin resistance (Brons et al., 2009; Cornier, Bergman, & Bessesen, 2006; Hagobian & Braun, 2006; Knudsen et al., 2012; C. C. Wang et al., 2013), an important precursor in the development of type 2 diabetes. However, maintenance of regular physical activity (Krogh-Madsen et al., 2014) or structured exercise training (Black, 2013; Hagobian & Braun, 2006; Walhin et al., 2013) appears to preserve insulin sensitivity despite excess intake, at least in the short-term. It has previously been suggested that total exercise duration (not intensity) is a more important factor for improving insulin action with exercise training (Houmard et al., 2004). However, a recent review by Kessler et al. (2012) found that HIIT leads to equal or superior improvements in insulin sensitivity in a variety of populations when compared to MICT, despite lower training times. A good illustration of this can be seen in the study by Nybo et al. (2010), which showed that just 40 min a week of HIIT yielded

similar improvements in 2-h glucose values during OGTT as compared with 150 min a week of MICT (Nybo et al., 2010). HIT may also be more effective than MICT for reducing postprandial spikes in glucose following subsequent meals (Little, Jung, Wright, Wright, & Manders, 2014). It is believed that HIIT may be superior to MICT due to higher muscle fiber recruitment (Edgett et al., 2013) and greater muscle glycogen depletion (Vollestad & Blom, 1985). Although previous studies have shown that exercise training may preserve insulin sensitivity despite excess caloric intake (Black, 2013; Walhin et al., 2013), it is unknown if HIIT is superior to MICT for maintaining insulin sensitivity and glycemic control.

Hypertriglyceridemia and hypercholesterolemia are independent risk factors for cardiovascular disease (Criqui et al., 1993; Stamler et al., 1986; Wilson et al., 1998). Both hypercaloric and eucaloric diets high in saturated fatty acids promote an atherogenic blood lipid profile (increased total cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides, while decreasing high-density lipoprotein cholesterol (HDL-C)) (Ortega et al., 2013). As little as 1-2 weeks of overfeeding (~ + 1,500 kcal/day) combined with physical inactivity has been shown to increase total and LDL-C levels significantly (Krogh-Madsen et al., 2014; Walhin et al., 2013). However, maintenance of regular physical activity (Krogh-Madsen et al., 2014) or daily exercise training (Walhin et al., 2013) during overfeeding appears to obliterate this effect despite a high-caloric intake. HIIT has been shown to be an effective strategy for attenuating fasting and postprandial TG (Ferreira et al., 2011; Freese, Levine, Chapman, Hausman, & Cureton, 2011) and may be more potent at reducing the incremental rise in postprandial TG compared with MICT or resistance training (Freese, Gist, & Cureton, 2014). Both HIIT and MICT

typically yield significant increases in HDL-C (Tambalis, Panagiotakos, Kavouras, & Sidossis, 2009), but improvements in HDL-C are more frequently observed with high-intensity exercise (Marrugat, Elosua, Covas, Molina, & Rubies-Prat, 1996; Tambalis et al., 2009).

Impaired endothelial function plays a primary role in the development of atherosclerosis (Vanhoutte, 2009) and is an independent risk factor for future cardiovascular disease (Green, O'Driscoll, Joyner, & Cable, 2008; Inaba, Chen, & Bergmann, 2010). The ingestion of a high-fat, high calorie meal has been shown to induce endothelial dysfunction (assessed by flow-mediated dilation of the brachial artery) for several hours post-meal (Vogel et al., 1997), suggesting that repeated intake of high-fat meals (as is typical in the Western Diet) may contribute to long-term endothelial dysfunction and atherosclerosis. Exercise training (both HIIT and MICT) has been shown to improve endothelial function (Currie, McKelvie, & Macdonald, 2012; Moholdt et al., 2012; Schjerve et al., 2008; Tjonna et al., 2008; Wisloff et al., 2007) with HIIT typically yielding greater improvements in FMD (Schjerve et al., 2008; Tjonna et al., 2008; Wisloff et al., 2007). Acute studies show that a bout of endurance exercise performed 16-18 h prior to ingestion of either a high-fat (Tyldum et al., 2009) or high-sugar meal (Weiss, Arif, Villareal, Marzetti, & Holloszy, 2008) can attenuate decreases in flow-mediated dilation (FMD). Furthermore, Tyldum et al. (2009) showed that high-intensity interval exercise was superior to moderate-intensity continuous exercise for preventing postprandial endothelial dysfunction, due in large part to higher antioxidant capacity during the 4-h postprandial period. Recent studies in mice (Park, Booth, Lee, Laye, & Zhang, 2012; Xu et al., 2011) and rats (La Favor, Anderson, Hickner, & Wingard, 2013)

reveals that exercise training during an 8-12 week period of high-fat feeding ameliorates coronary artery vascular dysfunction. Exercise training opposed the detrimental effects of a high-fat diet on vascular function including maintenance of eNOS phosphorylation, leptin sensitivity and redox balance in coronary arteries (Park et al., 2012). Furthermore, aortic constriction and relaxation was enhanced despite the presence of a high-fat diet due to exercise training (La Favor et al., 2013; Xu et al., 2011). The ability of regular exercise training to prevent endothelial dysfunction typically associated with periods of overfeeding or high-caloric intake in humans is unknown.

Overfeeding and high-fat diets have both been implicated as important contributors to hypertension (Muntzel, Al-Naimi, Barclay, & Ajasin, 2012; Stamler et al., 1986). Straznicky and colleagues (1993) showed that consuming a high-fat diet for 14 days increased systolic blood pressure (SBP) and heart rate reactivity in healthy, normotensive individuals. Similarly, 7 days of overfeeding (+50% of typical daily intake) has been shown to increase SBP in young healthy men (Walhin et al., 2013). Jakulj and colleagues (2007) demonstrated that a single high-fat meal can increase cardiovascular reactivity in young, normotensive individuals, with significant increases in SBP, DBP and total peripheral resistance following ingestion of the high-fat meal but not the low-fat meal. HIIT and MICT are equally effective treatment strategies for patients with hypertension or prehypertension (Cornelissen & Fagard, 2004; Cornelissen, Verheyden, Aubert, & Fagard, 2010; Kessler et al., 2012). However, it is unknown whether exercise training (HIIT or MICT) during periods of overfeeding or high caloric intake can prevent deleterious changes in blood pressure.

Aortic and peripheral artery stiffness are independent risk factors for prediction of cardiovascular events and all-cause mortality (Vlachopoulos, Aznaouridis, & Stefanadis, 2010). Western diets high in fat and sugar have been linked to increased arterial stiffness in humans (Hallikainen et al., 2013; Phillips et al., 2010; Rider et al., 2012) and animals (Bostick et al., 2015; Santana et al., 2014). Orr and colleagues (2008) demonstrated that 6-8 weeks of overfeeding (~1,000 kcal per day) to induce a 5 kg weight gain yielded a 13% increase in arterial stiffness and a 21% decrease in arterial compliance in young normal weight males. Furthermore, increases in arterial stiffness were strongly associated with increases in total abdominal fat ($r = 0.794$) and abdominal visceral fat ($r = 0.651$). A recent systematic review and meta-analysis (Ashor, Lara, Siervo, Celis-Morales, & Mathers, 2014), showed that aerobic exercise training (HIIT and MICT) improves both pulse wave velocity and augmentation index (measures of arterial stiffness). Furthermore, higher intensity exercise was associated with larger reductions in arterial stiffness (decreased augmentation index). These findings suggest that exercise training (both HIIT and MICT) may have the ability to attenuate or prevent the increases in arterial stiffness that typically accompany excess energy intake.

Cardiorespiratory fitness (CRF) is a strong independent predictor of all-cause and cardiovascular disease mortality (Kodama et al., 2009). Short-term reductions in physical activity coupled with overfeeding have been shown to reduce CRF (both absolute and relative VO_{2max}) in young healthy men (Knudsen et al., 2012; Krogh-Madsen et al., 2014; Krogh-Madsen et al., 2010). In contrast, maintaining regular physical activity levels (>10,000 steps per day) during 14 days of overfeeding fully preserved CRF (Krogh-Madsen et al., 2014). Two recent meta-analyses (Hwang, Wu, & Chou, 2011; Weston et

al., 2014) and one review (Kessler et al., 2012) suggest that HIIT is superior to MICT for improving CRF (assessed by VO_{2max} during a maximal exercise test). When combining all of the studies that included HIIT and MICT, Weston et al. (2014) found that HIIT yielded a superior 19.4% increase in relative VO_{2peak} versus a 10.3% increase in relative VO_{2peak} following MICT. However, it is unknown whether exercise training (HIIT or MICT) during periods of overfeeding or high caloric intake can improve CRF.

CHAPTER 3

METHODS AND MATERIALS

Subjects

Four hundred and ninety-two individuals completed the online pre-screening survey (Qualtrics Survey Software; Qualtrics, Provo, UT, USA) for participation in this study. Thirty-one males met the inclusion criteria for participation and attended an in-person screening visit. Three subjects dropped out of the study prior to baseline testing and one subject was excluded due to diabetes diagnosis (blood glucose > 126 mg/dl) at screening. The CONSORT diagram for this study is depicted in Figure 1. Twenty-seven (n = 27) sedentary overweight or obese males (age, 18-50 years) participated in and completed the study. Subject characteristics are listed in Table 1.

Inclusion criteria included age between 18-50, overweight/obese (>25 kg/m^2), capable of performing vigorous physical activity and capable of eating two donuts per day, six days per week for the duration of the study. Exclusion criteria included: smoking, blood pressure >160/100 mmHg, diagnosed or undiagnosed diabetes, heart disease, severe obesity (>45 kg/m^2), acute/chronic dieters, dietary supplements, medications for the treatment of diabetes, heart disease, cholesterol, engaging in regular physical activity. Sedentary was defined as not engaging in a regular exercise program or not accumulating 30 minutes or more of moderate physical activity on most days of the week (ACSM). All subjects provided informed written consent and passed the PAR-Q before starting the study. This study was approved by the Arizona State University Institutional Review Board (IRB #: 00001517; Appendix A). All procedures were carried out as per the declaration of Helsinki.

Table 1. Subject characteristics at baseline (mean ± SD).

	Control (n=9)	**MICT (n=8)**	**HIIT (n=10)**
Age (years)	27.9 ± 8.4	29.6 ± 7.4	30.3 ± 7.0
Height (cm)	177.8 ± 7.5	179.7 ± 10.2	178.1 ± 5.5
Weight (kg)	93.4 ± 12.0	97.2 ± 19.3	95.7 ± 7.6
Body Mass Index (kg/m²)	29.6 ± 3.9	30.0 ± 4.7	30.2 ± 3.0
Body Fat Percentage (%)	31.5 ± 5.9	32.4 ± 5.8	30.5 ± 4.5
Fat Mass (kg)	29.5 ± 8.5	28.2 ± 6.5	30.4 ± 9.1
Fat-Free Mass (kg)	64.2 ± 5.9	64.0 ± 10.2	68.7 ± 6.1
VO_{2peak} (L/min)	3.0 ± 0.5	3.1 ± 0.7	3.2 ± 0.5
VO_{2peak} (ml/kg/min)	31.4 ± 4.1	32.8 ± 4.8	33.2 ± 6.9

MICT= Moderate-intensity continuous training; HIIT = High-intensity interval training. No significant differences were detected between groups at baseline.

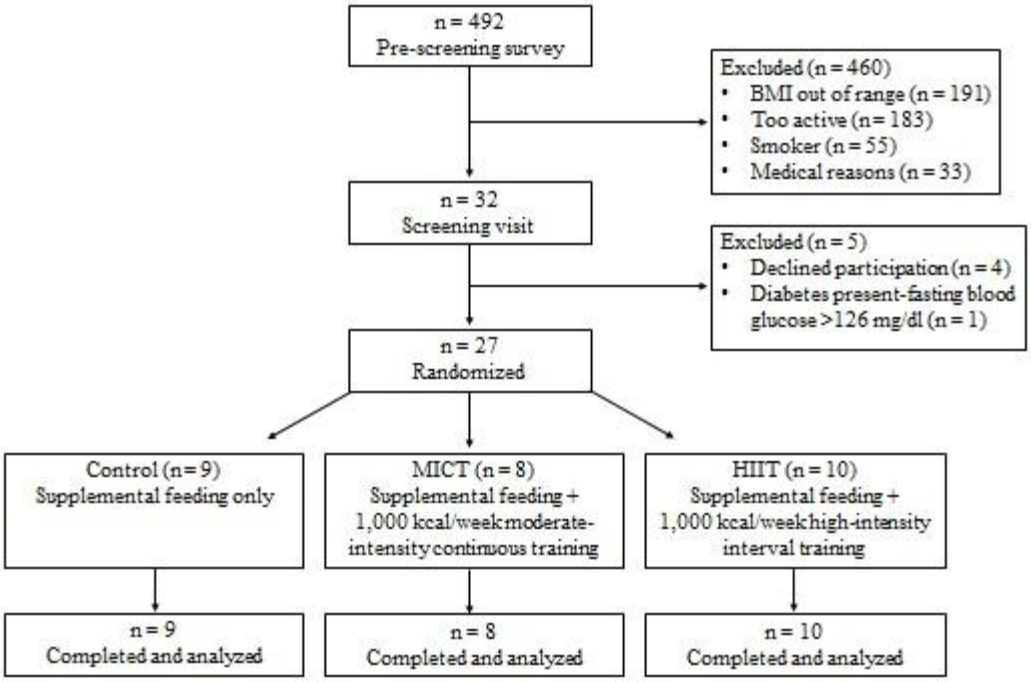

Figure 1. CONSORT diagram

Recruitment and Screening

Our main target population was young, overweight/obese sedentary males from the four Arizona State University campuses and the Greater Phoenix Area (Phoenix, AZ, USA). Successful recruitment efforts were facilitated through distribution of flyers (Appendix C) and advertisements across the four ASU campuses as well as listserv emails to all ASU departments. Participants were informed that they were free to withdraw from the study at any time, that nonparticipation would not affect any services, and that their names would not appear on study materials. Unique 4-digit numbers were used to code data for confidentiality.

All participants who responded to the recruitment flyer were sent an email attachment with pre-screening questions and a physical activity readiness questionnaire (PAR-Q) (Appendix B) as part of the Qualtrics Online Survey System (Qualtrics Survey Software; Qualtrics, Provo, UT, USA) to establish eligibility for participation. Participants were asked about age, height, weight, gender, and then asked to answer several "yes" or "no" questions related to current smoking status, current participation in an exercise training program, current participation in calorically restrictive diets, whether they recently (last 3 months) had weight loss of >10 pounds, and whether they did more than 2 days a week of moderate-physical activity. All individuals who had previously been diagnosed or told that they have hypertriglyceridemia or hypercholesterolemia by a physician were excluded from the study. Lastly, if subjects answered "yes" to any question on the PAR-Q, they were not allowed to participate unless they obtained a physician's release.

Participants who met the eligibility requirements after completing the pre-screening survey were asked to report to the Healthy Lifestyles Research Center in ABC 1 on the ASU Downtown Campus and provided with a copy of the consent form (Appendix A). All aspects of the study were explained and informed written consent was obtained prior to enrollment in the study. Participants also filled out and signed the PAR-Q (Appendix B) to ensure that they were suitable candidates for enrollment. Those who decided to participate after signing the consent form had their height, weight and blood pressure measured to ensure that they met the BMI and blood pressure criteria for participation (Appendix D). Fasting capillary blood glucose was obtained using the fingerstick method to check for undiagnosed diabetes (blood glucose $\geq$ 126 mg/dl) with a One Touch Ultra Glucose Meter (LifeScan, Milpitas, CA, USA). Individuals who met the criteria for participation were given a physical activity monitor (SenseWear Armband; Model: WMS, Bodymedia, Pittsburgh, PA, USA) (SenseWear Armband, Pittsburgh, USA) and Three-day Food Record (Appendix E) to assess habitual physical activity and diet prior to participation in the intervention.

Research Design and Protocol

A randomized parallel group design was used for this study. Participants were randomly assigned to either a supplemental feeding group only (Control), supplemental feeding plus 1,000 kcal of moderate-intensity continuous training group (MICT) or, supplemental feeding plus 1,000 kcal of high-intensity interval training (HIIT) group for the 4-week intervention period. The 4-week study duration was selected in order to best simulate the winter holiday period which has been identified as a high-risk period for

weight gain due to overfeeding and sedentary behavior (Stevenson et al., 2013; Yanovski et al., 2000).

All study participants reported to the laboratory for testing at baseline and 4 weeks early in the morning following a > 10 h overnight fast. Participants were instructed to refrain from exercise, caffeine, alcohol and dietary supplements for 48 hours prior to this testing visit. Body composition, arterial stiffness, endothelial function, glycemic control and cardiorespiratory fitness were all measured in order at each testing visit. After the assessment of glycemic control, all participants were fed a small lunch consisting of a Clif Bar and Lay's Potato Chips (410 kcal) ~10 minutes prior to assessing cardiorespiratory fitness.

Following completion of baseline testing, participants were randomly assigned to control, MICT or HIIT intervention groups. Post-testing was carried out >48 hours following the last exercise training (MICT or HIIT) session to avoid carryover effects from the last bout of exercise. Participants in the control group reported to our lab 48 hours after their last supplemental feeding. The order and time of day of these testing procedures was held constant within-subject relative to baseline to reduce the impact of diurnal variations in the clinical variables measured.

Body Composition Testing

Standing height (cm) was assessed by a digital stadiometer (Seca 284, Seca, Hamburg, Germany). The Seca 284 digital stadiometer and scale is a high capacity scale that can handle up to 300 kg with graduation for weight of 0.05 kg and height 0.01cm. Waist circumference was taken at the umbilicus using a standard Gulick tape measure. The average of two consecutive measurements was used for height and waist

circumference assessments. Body weight and composition was determined at baseline and 4 weeks using Dual-energy X-ray Absorptiometry (DXA) (Lunar iDXA, GE Healthcare, Madison, WI, USA). All DXA scans were analyzed using enCORE version 13.6 software to quantify total body fat percent, and total fat mass and fat-free mass (kg). The Lunar iDXA also possesses a tool for accurately quantifying visceral adipose tissue (VAT) mass and volume over the android region of the body using CoreScan software (GE Healthcare, Madison, WI, USA). A certified radiology technician calibrated the DXA before each day of testing and performed all of the DXA scans. Participants removed shoes and all jewelry prior to each scan.

DXA is considered by many experts to be the practical gold standard and a criterion method for measuring body composition (M. P. St-Onge et al., 2004). The Lunar iDXA has a high weight limit (204 kg) and narrow angle fan beam DXA system which improves image clarity and reduces precision error. Validation studies show high test-retest reliability (coefficient of variation 0.8 to 2.8%) for the measurement of body fat, fat-free mass and bone mineral density across a wide range of BMI's (Carver, Christou, & Andersen, 2013; Toombs, Ducher, Shepherd, & De Souza, 2012). DXA also exhibits good levels of agreement against the 4-comparment model (1-2% difference), a tool considered to be the gold standard for assessing body composition (Fogelholm & van Marken Lichtenbelt, 1997; Toombs et al., 2012). The iDXA's CoreScan software has also demonstrated good precision for quantifying visceral adipose tissue (within 58g for repeated assessment of VAT mass of 1.11 kg; 5% CV) in a cohort of obese women (Rothney et al., 2013). Furthermore, the Lunar iDXA with CoreScan shows strong agreement (r^2=0.957) against Computed Tomography (the gold standard for quantifying

visceral fat) for quantifying visceral fat in both genders and across a wide range of BMI's (Range: 18.5-40 kg/m^2) (Kaul et al., 2013).

Energy Balance Equations

To better assess overall changes in energy balance within the body during the 4-week intervention, change in fat and lean tissue quantities were inserted into a formula (King, Hopkins, Caudwell, Stubbs, & Blundell, 2009; Sawyer, Bhammar et al., 2015) to determine energy balance:

[1] $EB = (\Delta \text{ lean mass [kg]} \times 1{,}100 \text{ kcal}\cdot\text{kg}^{-1}) + (\Delta \text{ fat mass [kg]} \times 9{,}540 \text{ kcal}\cdot\text{kg}^{-1})$

The theoretical change in energy balance during the intervention alone (donuts minus exercise) was calculated as:

[2] Theoretical EB (intervention) = (Energy intake donuts) ─ (energy expenditure exercise training)

To assess spontaneous changes in energy intake or energy expenditure during the intervention, data from food records and accelerometers were entered into the following equations, respectively:

[3] Δ Habitual Energy Intake (food records) = (Daily post energy intake) ─ (daily pre energy intake) X 28 days (intervention length)

[4] Δ Habitual Energy Expenditure (accelerometer) = (Post energy expenditure) ─ (pre energy expenditure) X 28 days (intervention length)

Overall theoretical predicted change in energy balance during the intervention was calculated as follows:

[5] Δ Overall Theoretical Predicted EB = (intervention [2]) + (Δ habitual energy intake [3] ─ Δ habitual energy expenditure [4])

To quantify potential compensation in habitual dietary intake and physical activity during the intervention, overall theoretical change in energy balance was subtracted from actual change in energy balance from DXA data as follows:

[6] Total energy compensation = Actual Δ EB [1] ─ Overall Theoretical Predicted Δ EB [5]

Blood Pressure and Arterial Stiffness

Upon completion of body composition analysis, all subjects lay down in a dimly lit, climate-controlled room and had blood pressure measured using a Dinamap GE PRO 400 V2 (GE Medical Systems Information Technologies, Inc., Milwaukee, WI, USA) automated blood pressure monitor at 0, 10 and 15 min after initially laying down to ensure that hemodynamic stability had been achieved. Thereafter, an appropriately sized blood pressure cuff was placed on the left arm and central and peripheral blood pressures

were assessed using the non-invasive SphygmoCor system (AtCor Medical, Sydney, Australia).

The SphygmoCor XCEL PWA device provides valid assessments of peripheral blood pressure, central aortic blood pressure, augmentation indices (Chen et al., 1997; Karamanoglu, O'Rourke, Avolio, & Kelly, 1993; Pauca, O'Rourke, & Kon, 2001; Savage, Ferro, Pinder, & Tomson, 2002; Wilkinson et al., 1998). The SphygmoCor XCEL system records brachial systolic and diastolic pressure, and then captures the patient's brachial waveform. The brachial waveform is then analyzed by the SphygmoCor Brachial GTF software to provide a Central aortic waveform, and Central Blood pressure measurements such as Central Aortic Systolic BP, Central Pulse pressure (Pulse Wave Analysis) and Augmentation indices are also displayed. Three measurements were taken with the SphygmoCor device, with the 2 closest values being averaged to obtain peripheral and central blood pressures, as well as augmentation indices (Appendix I). The Augmentation Index (AIx) was calculated as the difference between the first and second systolic peaks (augmentation pressure) of the ascending aortic waveform divided by the difference between central systolic and diastolic pressures. In addition, since AIx is influenced by heart rate, a normalized version of AIx at heart rate of 75 bpm (AIx @ 75) was used.

To obtain carotid femoral pulse wave velocity (cf-PWV), a blood pressure cuff was placed around the thigh of the patient and inflated to sub-systolic pressure (<150 mmHg) to capture the femoral artery waveform, and a tonometer pressure sensor was used to capture the Carotid waveform. The Pulses were collected over a pre-set time, the Pulse transit time which is the time that the pulse takes to travel from the carotid artery to the femoral artery were assessed. The distance between the Carotid and femoral arteries

was measured, and the pulse wave velocity automatically determined by dividing the distance by the Pulse transit time. Three measurements were taken with the SphygmoCor device, with the 2 closest values being averaged to obtain PWV (Appendix I).

Endothelial-dependent Vascular Function

Endothelial function was assessed by flow-mediated dilation (FMD) of the brachial artery using high-resolution 2D and Doppler ultrasound (Terason t3000CV Ultrasound, Terason, Burlington, MA) with a linear-array transducer at a frequency of 12 MHz, following current guidelines (R. A. Harris, Nishiyama, Wray, & Richardson, 2010; Thijssen et al., 2011). Measurements were made in a dimly lit, climate-controlled room after 20 minutes of supine rest. All brachial artery images were taken on the subject's left arm (immobilized) in the longitudinal plane, proximal to the antecubital fold. Continuous Doppler velocity assessments were obtained using the lower possible insonation angle (<60 degrees) with ultrasound. The ultrasound procedure was individualized to optimize image clarity and avoid arterial branching. Probe location and image settings (depth, gain, compression and rejection) for the initial assessment were recorded and repeated for subsequent testing visits to ensure high reproducibility within-subject (Appendix I). A 1-min, B-mode video was captured to determine baseline brachial artery diameter. Following baseline assessment, an automated blood pressure cuff (Hokanson E20 Rapid Cuff Inflator, Hokanson Inc., Bellevue, WA, USA) was placed 2 cm distal to the antecubital fold and inflated to >200 mmHg (or greater than 50 mmHg above systolic blood pressure) for a 5-min occlusion. Digital videos were recorded for 1-min prior to cuff release and for at least 3-min following cuff release to assess peak artery dimeter,

blood velocity and shear rate. Arterial diameters were calculated as the distance between anterior and posterior walls of the intima-lumen interface.

FMD was defined as the change in arterial diameter from rest to peak dilation as a percentage of baseline diameter. Ultrasound images were recorded at 30 frames/second using Camtasia software (TechSmith, Okemos, MI, USA). All FMD's were performed by the same well-trained sonographer. All ultrasound images were analyzed using semi-automated edge-detection software (Woodman et al., 2001) by a single investigator who was blinded to the time and experimental condition of all images. Shear rate AUC and blood velocity (cm/s) were assessed from cuff release to peak dilation for each FMD (R. A. Harris et al., 2010; Thijssen et al., 2011). All images (n = 108) were analyzed in duplicate. Intra-user reliability was as follows: baseline diameter (CV% = 0.22%, ICC = 0.99), peak diameter (CV% = 0.21%, ICC = 0.99) and FMD% (CV% = 4.20%, ICC = 0.97). A second investigator who was randomized and blinded, analyzed a subset of the images (n=40) to assess inter-observer reliability. Inter-observer reliability was as follows: baseline diameter (CV% = 0.94%, ICC = 0.98), peak diameter (CV% = 1.60%, ICC = 0.96) and FMD% (CV% = 8.2%, ICC = 0.97).

Glucose and Lipid Metabolism

Euglycemic clamp and intravenous glucose tolerance test (IVGTT) are considered "gold-standard" assessments of insulin sensitivity (Bergman, Ider, Bowden, & Cobelli, 1979). However, these measurements are expensive, time-consuming, invasive and impractical (Staten & Kelley, 2014). In contrast, the oral glucose tolerance test (OGTT) is an inexpensive and practical method for assessing insulin sensitivity and Beta-cell function (Abdul-Ghani, Matsuda, Balas, & DeFronzo, 2007). The OGTT more closely

emulates daily habits of nutrient ingestion since it directly feeds the gut and evokes incretin and other gut hormonal responses versus intravenous bolus and continuous infusion of glucose utilized in the euglycemic clamp and IVGTT which do not (Staten & Kelley, 2014). Furthermore, previous studies examining the effects of overfeeding and altered physical activity levels have utilized the OGTT to assess changes in insulin action and glycemic control (Krogh-Madsen et al., 2014; Walhin et al., 2013).

For this study, all participants completed a 2-h oral glucose tolerance test (OGTT) using 75 g of anhydrous glucose solution dissolved in water. A small polyethylene catheter was placed into an antecubital vein and venous blood samples were collected at baseline and every 30 min (─ 30, 0, 30, 60, 90, 120 min, relative to glucose ingestion). After each blood draw during the OGTT, the blood was placed into appropriately labeled vacutainers, processed and stored at ─80º C until assayed. Serum glucose and lipids (total cholesterol, high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), and triglycerides) were analyzed using an automated chemistry analyzer (Cobas C111; Roche Diagnostics, Indianapolis, IN) using colorimetric enzymatic reagents. Measured intra-assay CVs were 0.46% for total cholesterol, 0.45% for HDL-c, 0.52% LDL-c, 0.79% for triglycerides and 0.46% for glucose. Serum insulin was measured using the ultrasensitive human radioimmunoassay kit (Millipore Corporation, Billerica, MA). Measured intra-assay CV for insulin was 4.9%.

OGTT Calculations

Total and incremental glucose and insulin area under the curve (tAUC and iAUC respectively) and OGTT-derived indices of insulin action were used to assess changes in glycemic control during the intervention. The trapezoidal rule was used to calculate

tAUC by subtracting zero from the AUC and iAUC for glucose and insulin by subtracting the fasting value from AUC (Wolever & Jenkins, 1986). Insulin sensitivity index (ISI) was estimated by Matsuda Index, which strongly correlates with the rate of whole-body glucose disposal during euglycemic-hyperinsulinemic clamp (Matsuda & DeFronzo, 1999):

[6] $ISI = 10{,}000 \div \sqrt{((\text{fasting GLUC} * \text{fasting INS})(\text{mean 2-h GLUC} * \text{mean 2-h INS}))}$

Abdul-Ghani and colleagues (2007) recently validated OGTT-derived indices of hepatic insulin resistance index (IRI) against euglycemic-hyperinsulinemic clamp and found good to moderate agreement in subjects with normal and impaired glucose control. The product of glucose and insulin tAUCs during the first 30 min of the OGTT was used to calculate the hepatic IRI:

[7] $\text{hepatic IRI} = (\text{Glucose tAUC}_{0\text{-}30\text{min}} \times \text{Insulin tAUC}_{0\text{-}30\text{min}})/1000$

The early insulin response (insulinogenic index (IGI)) was calculated as the ratio of the change in insulin to the change in glucose during the 1st 30 min of the OGTT (Abdul-Ghani et al., 2007):

[8] $IGI = (\text{Insulin iAUC}_{0\text{-}30\text{min}} \div \text{Glucose iAUC}_{0\text{-}30\text{min}})$

Beta-cell function was estimated using the oral disposition index (DI), which has been validated against the IVGTT (Retnakaran, Qi, Goran, & Hamilton, 2009):

[9] DI (insulin secretion X insulin sensitivity) = IGI X ISI (Matsuda Index)

The homeostatic model assessment (HOMA-IR) score was calculated as:

[10] (HOMA-IR = glucose (mmol/L) x insulin (μU/ml)/22.5)

Cardiorespiratory Fitness

Peak Oxygen uptake (VO_2 peak) was measured during an incremental exercise test performed on electronically braked cycle ergometer (Viasprint 150P; Ergoline, Bitz, Germany) using indirect calorimetry (TrueMax 2400; Parvo Medics, Sandy, UT, USA).

At baseline and 4 weeks, subjects were equipped with an oronasal mask fitted with a standard non-rebreathing valve (Hans Rudolph, Shawnee, KS, USA) and heart rate monitor (Polar H7; Polar Electro OY, Kempele, Finland). Ventilation, gas exchange and HR were monitored continuously with the Parvo Medics TrueMax 2400 computerized metabolic measurement system. A standard 3-point calibration was performed before each test per manufacturer recommendations. This system has been previously validated against the Douglas bag method with high levels of accuracy and precision for gas-exchange measurement during exercise (Crouter, Antczak, Hudak, DellaValle, & Haas, 2006).

After 2 minutes of seated rest, subjects pedaled at a cadence of their choice (60-80 rpm) for 5 minutes at 50 W on an electronically braked cycle ergometer. After this warm-up, power increased continuously in a ramp fashion (1 W every 2 s) until each subject reached volitional fatigue despite strong verbal encouragement. After a 5- to 10-minute cool-down phase of cycling at 50 W, subjects performed a verification phase on the cycle ergometer at a constant power of 100% of maximum power achieved during the incremental ramp test until they reached volitional exhaustion (Sawyer, Tucker, Bhammar, & Gaesser, 2015; Tucker, Sawyer, Jarrett, Bhammar, & Gaesser, 2015). Subjects were asked to maintain their previously selected cadence and pedal for as long as possible during the verification phase. After completion of the verification phase, all subjects completed a 5-minute cooldown at 50 W.

VO_{2peak} was defined as the average of the two highest consecutive 15-second averages achieved for VO_2 during either the ramp or verification phase of the maximal exercise test. Peak heart rate (HR_{peak}) was determined using the highest HR achieved during either the ramp or verification phase.

Habitual Dietary Intake and Physical Activity

All subjects were asked to keep track of their habitual dietary intake by filling out a Three-Day Food Record (Appendix E) at baseline (pre-intervention) and during the last week of the intervention. Dietary intake was recorded on two weekdays and one weekend day. Habitual energy and macronutrient intakes were determined by averaging diet records at each time point and analyzed (Diet Analysis Plus 10.0; Cengage, Independence, KY).

Upon consent, participants' daily total energy expenditure (TEE), step-count, average daily metabolic equivalents (METs) and number of sedentary-, and moderate-intensity physical activity minutes were measured by SenseWear armband (SWA; Model: WMS, Bodymedia, Pittsburgh, PA, USA) for 7 days prior to baseline testing and then repeated during the 4th week of the intervention. The SenseWear armband (SWA) is a wireless, non-invasive physical activity monitor that contains a triaxial accelerometer and four heat sensors (Smith, Lanningham-Foster, Welk, & Campbell, 2012). The SWA has been previously validated for the assessment of physical activity and energy expenditure during both free-living and structured physical activity with good levels of agreement against criterion measures (Jakicic et al., 2004; Johannsen et al., 2010; M. St-Onge, Mignault, Allison, & Rabasa-Lhoret, 2007; Tucker, Bhammar, Sawyer, Buman, & Gaesser, 2015). The armband was worn on the upper posterior aspect of the left arm for all subjects in accordance with manufacturer recommendations. Subjects were instructed to wear the armband throughout the day but permitted to remove the armband at night in order to avoid discomfort during sleep. In addition, the armband was removed prior to exercise training in subjects randomized to the exercise training groups. To ensure precision, time of day and a 12-hour assessment period were held constant within-subject at baseline and 4 weeks.

Supplemental Feeding

All subjects were instructed to maintain their current diet and supplement with 2 donuts per day, 6 days per week, for 4 weeks to simulate typical excess energy consumption during an extended holiday period. Donuts were purchased by our research team at a local Dunkin Donuts on Monday, Wednesday and Friday morning of each week

and given to participants. On each occasion subjects were given 4 donuts to consume over the next two days. Subjects were instructed to consume the donuts as snacks between typical meals. Participants were provided with a menu of donut options (Appendix K) so that each participant was able to choose the types of donuts that he would like most to consume. All donuts contained between 250 and 350 calories, of which at least 70% of total calories was fat and sugar. The average daily fat-sugar supplement (2 donuts) amounted to 606 kcal/day (excludes 1 rest day each week). Nutrition information for the donuts was obtained from the manufacturer website (Dunkin Donuts, Canton, MA, USA). The energy content and macronutrient profile of the total supplementary feeding during the 4-week intervention is provided in Table 2.

Table 2. Supplemental feeding nutrition information (mean ± SD)

	Control (n=9)	MICT (n=8)	HIIT (n=10)	P-value
Donuts				
Total Energy (kcal)	14,554 ± 572	14,542 ± 398	14,651 ± 218	0.85
Carbohydrate (g)	1,686 ± 61	1,705 ± 54	1,688 ± 54	0.75
Fat (g)	815 ± 41	807 ± 20	805 ± 39	0.82
Protein (g)	153 ± 5	158 ± 7	154 ± 3	0.24
Saturated Fat (g)	360 ± 22	355 ± 10	355 ± 17	0.75
Fiber (g)	50 ± 3	54 ± 5	52 ± 3	0.15
Sugar (g)	731 ± 42	749 ± 19	739 ± 34	0.56
Macronutrient Content				
Carbohydrate (%)	46 ± 1	46 ± 1	46 ± 1	0.76
Fat (%)	50 ± 1	50 ± 1	50 ± 1	0.92
Protein (%)	4 ± 0	4 ± 1	4 ± 0	0.17

P-values represent between-group differences.

MICT= Moderate-intensity continuous training; HIIT = High-intensity interval training.

Exercise Training

Participants randomized to either of the exercise protocols completed 16 exercise training sessions over a period of 4 weeks (4 days/ week). All exercise training was supervised (Appendix F and G) and performed on mechanically-braked cycle ergometers (Monark Ergomedic 828E, Monark, Sweden). Heart rate was monitored continuously using a heart rate monitor (Polar H7; Polar Electro OY, Kempele, Finland) and recorded during all exercise training sessions. The aerobic exercise training protocols consisted of either: (1). 1,000 kcal per week of moderate-intensity continuous training (MICT) at 50% VO_2 peak on a cycle ergometer, or (2). 1,000 kcal per week of high-intensity interval training (HIIT) consisting of 8-11, 1-minute intervals at 90-95% HR_{peak}, separated by 1 minute of light active recovery (~50 W).

Exercise duration for each participant was individualized based on VO_{2peak} to ensure that exercise protocols were isoenergetic and matched at 250 kcal per session or 1,000 kcal per week. This was achieved in MICT by multiplying absolute VO_{2peak} (L/min) by 50% and then multiplying by 5 kcal/L to obtain energy expenditure in kcal/min. To calculate exercise duration for each participant, 200 kcal was divided by the previously calculated kcal/min to obtain exercise duration in minutes. To achieve exercise duration for HIIT, I multiplied absolute VO2peak (L/min) by 67% and then multiplied by 5 kcal/L to obtain energy expenditure in kcal/min. Previous work in our lab illustrates that a HIIT protocol of this nature (10, 1-min intervals) yields a mean VO_2 of 67% of VO_{2peak} (Tucker, Sawyer et al., 2015). To calculate exercise duration for each participant, 200 kcal was divided by the previously calculated kcal/min to obtain exercise duration in minutes. Each exercise session began with a 5-minute warm-up (50 W), and

finished with a 5-minute cooldown (50 W). Warm-up and cool-down duration were estimated to yield a total energy cost of 50 kcal based on previous data from our lab examining VO_2 during cycling at 50 W in overweight and obese men.

Subjects randomized to the control group participated in the supplemental feeding intervention only and were instructed to maintain habitual diet and exercise patterns for the duration of the study. In addition, subjects in the control group were offered 4 weeks of free exercise training at the completion of the study. If they decided to participate, the subjects had their choice of either of the exercise training interventions described above. The only additional assessment would be body weight at the completion of those 4 weeks of optional exercise training.

To assess whether there was a difference in perceived enjoyment between the two exercise training groups (HIIT or MICT), each subject completed the Physical Activity Enjoyment Scale (PACES) (Bartlett et al., 2011; Kenzierski, 1991) (Appendix J). This scale has been shown to be a valid measure of quantifying perceived enjoyment of exercise (Bartlett et al., 2011; Kenzierski, 1991). Each item on the PACES is rated on a 7-point bipolar scale with 4 representing a neutral point in terms of how much the respondent enjoyed the exercise. Subjects filled out the PACES within 20 minutes of completing their last bout of exercise.

Sample Size Power Estimates

The sample size was calculated for the primary aim to detect a 1.9 kg (2.5%) difference of body weight between control and exercise conditions using G*Power 3.0 software (Faul, Erdfelder, Lang, & Buchner, 2007). I assumed 95% Power at 0.05% alpha level of significance (two-sided). Estimates were based upon a pilot study

performed recently in Dr. Gaesser's lab, which examined the effects of an acute exercise intervention to prevent weight gain associated with overfeeding (Black, 2013). Based on these parameters the recruitment goal of 36 participants was calculated to give us 95% power to detect 1.9 kg (2.5%) difference between control and exercise conditions for body weight changes. Even with a ~17% drop-out rate, completion of 30 participants would yield 90% power at a 0.05 alpha level of significance (two-sided).

Statistical Analysis

All variables were checked regarding their normal distribution using the Shapiro-Wilk test and logarithmically transformed if appropriate. All statistical procedures were performed by SPSS Software (SPSS 22.0, IBM, Armonk, NY). All P values were 2-sided, and values <0.05 were considered statistically significant. P-values <0.20 were considered a trend.

The effect of time (before and after) and group (Control, MICT or HIIT) on body weight, fat mass, endothelial function, and habitual diet and exercise were assessed by Two-Way Repeated Measures ANOVA to detect if there was a significant time-group interaction present. Baseline moderate physical activity minutes (as assessed by accelerometer) was included as a covariate in a Two-Way RM ANCOVA to assess statistical differences in blood pressure, arterial stiffness, blood lipids and OGTT-derived indices. If the sphericity assumption was violated (Greenhouse-Geisser $\varepsilon < 0.75$), degrees of freedom (df values) for within-subject were adjusted using Greenhouse-Geisser correction. Sidak correction for multiple comparisons was used for post-hoc pairwise comparisons. One-Way ANOVAs were run to check for differences between conditions for descriptive variables at baseline and dietary composition of supplemental feedings

during the intervention. In addition, One-Way ANOVAs were run to assess whether there were significant differences in any of the change in energy balance variables. An unpaired T-test was used to assess differences between PACES and exercise time between exercise protocols. Pearson correlations were used to assess associations between actual energy balance as observed by DXA and theoretical energy balance.

It was recently described that inadequate scaling for the FMD variable would be present if the upper confidence interval (CI) of the regression slope of the relationship between logarithmically transformed base and peak diameters was < 1 (Atkinson, Batterham, Thijssen, & Green, 2013). If this were to occur, FMD (%) may not be an appropriate measure to assess endothelial function due to the potential for bias between conditions due to differences in baseline arterial diameter. For the current study, a linear regression of logarithmically transformed base and peak diameters yielded a regression slope upper confidence interval >1 ($\beta \pm SE = 0.94 \pm 0.04$; 95% CI = 0.86 to 1.02). Therefore, in accordance with the guidelines outlined by Atkinson et al. (2013), allometric scaling was deemed unnecessary and the % FMD variable was utilized as the dependent variable. To adjust for potential differences in shear rate between subjects, FMD was also normalized by dividing % FMD by shear rate to create FMD/shear rate. Both FMD% and FMD/shear rate were included as dependent variables for analyses as per guidelines (R. A. Harris et al., 2010).

Estimated effect sizes between conditions were calculated with the following formula (Morris, 2008):

[11] $$\text{Effect size} = \frac{(\text{Mean difference}_{(\text{post-pre})}\ \text{group 1} - \text{mean difference}_{(\text{post-pre})}\ \text{group 2})}{\text{Pooled Baseline Standard Deviation}}$$

CHAPTER 4

RESULTS

Habitual Physical Activity and Dietary Intake

Results for changes in habitual physical activity and diet within group are presented in Table 3. There was no significant change in objectively measured habitual physical activity during the intervention. In the control group, habitual carbohydrate intake decreased significantly (─47 g; p=0.02) and there was a trend towards a significant reduction in total energy intake (─ 239 kcal; p=0.06). Habitual dietary intake was not significantly altered in the MICT or HIIT group.

Body Composition

Results for changes in body composition as assessed by DXA are presented in Table 4. There was a significant time x group interaction for body weight during the intervention (p=0.03), with a significant increase within the HIIT group (+1.4 kg; p=0.002) and a trend towards an increase in body weight within the control group (+0.9 kg; p=0.07). In contrast, body weight was unchanged in the MICT group (─0.6 kg; p=0.39). Fat mass was relatively unchanged in control and MICT groups, while those in the HIIT group displayed a trend towards increased fat mass after the intervention (+0.6 kg; p=0.11). Total lean mass increased significantly within the HIIT group (+0.9 kg; p=0.02) and trended towards a significant increase within the control group (+0.7 kg; p=0.11). Total lean mass did not change in the MICT group (p=0.90). There was considerable individual variability in the changes in body weight (-2.7 to 3.7 kg) (Figure 2), fat mass (-2.2 to 1.7 kg) (Figure 3) and lean mass (-1.6 to 2.5 kg) (Figure 4) across all groups during the 4-week intervention.

For changes in regional adiposity (Table 4), the MICT group demonstrated a trend towards a significant reduction in android (−0.12 kg; p=0.09) and gynoid fat mass (−0.12 kg, p=0.07) within group, while the control group was unchanged or demonstrated a small non-significant increase (Table 4). There was a trend towards a significant increase in trunk fat (+0.5 kg; p=0.08) and android fat mass (+0.10 kg, p=0.09) in the HIIT group. Visceral adipose tissue (VAT) increased significantly in the HIIT group (+88 cm^3, p=0.04) but did not change in the MICT group (−11cm^3; p=0.81) and the control group (+2 cm^3; p=0.97).

Energy Balance

Actual changes in energy balance from the DXA revealed a significant difference between MICT (−3,449 ± 11,590 kcal) and HIIT (+5,942 ± 5,969 kcal) (Figure 5) (p=0.04). Control (+2,228 ± 9,494 kcal) was not significantly different from MICT (p=0.21) or HIIT (p=0.38). Large individual variability in the actual changes in body energy balance were observed within and across all conditions (−19,884 to 17, 241 kcal) (Figure 6).

Theoretical (predicted) change in energy balance based on the intervention alone (Energy value of donuts minus energy value of all exercise sessions (or no exercise)) revealed a significantly greater positive energy balance in control (+14,554 ± 572 kcal) than MICT (+10,542 ± 365 kcal) or HIIT (10,651 ± 299 kcal) ($p < 0.001$) (Figure 7). For changes in habitual energy intake (based on food records), the control group (−6,681 ± 8,861 kcal) showed the biggest compensation in dietary intake compared with MICT (−1,054 ± 9,565 kcal, p=0.25) and HIIT (−1,202 ± 11,343 kcal, p=0.26) (Figure 8). Changes in habitual energy expenditure (based on accelerometer) were minor (Control: −

375 ± 3,074 kcal; MICT: +562 ± 5,512 kcal; HIIT: +282 ± 4,546 kcal) and not significantly different between groups (p=0.90) (Figure 9). Considerable individual variability for changes in habitual energy intake (Figure 10) and habitual energy expenditure (Figure 11) was evident within and across all conditions.

Overall theoretical (predicted) change in energy balance (energy value of donuts ─ energy value of exercise training + energy value of change in habitual energy intake ─ energy value of change in habitual energy expenditure) was not significantly different between groups (p=0.98) (Figure 12). Furthermore, there was no significant difference between the actual minus theoretical (predicted) change in energy balance variable between conditions (p=0.29) (Figure 13). However, conditions still exhibited large differences (Control: ─6,013 ± 12,221 kcal; MICT: ─12,404 ± 16,249 kcal; HIIT: ─3,188 ± 8,294 kcal). Furthermore, the individual variability within and across conditions (─36,720 to +15,195 kcal) was large.

There was a weak, non-significant association between overall theoretical change in energy balance and actual changes in energy balance from DXA ($r = 0.124$, $p = 0.54$).

Table 3. Habitual physical activity and dietary intake (mean ± SD).

	CON (n=9)			MICT (n=8)			HIIT (n=10)		
	Before	After	*P*	Before	After	*P*	Before	After	*P*
Habitual physical activity									
TEE (kcal/day)	1,878 ± 377	1,865 ± 312	0.80	2,045 ± 357	2,065 ± 385	0.72	1,947 ± 270	1,957 ± 212	0.84
Steps/day	6,417 ± 1,435	6,352 ± 1,583	0.92	7,038 ± 2,769	7,317 ± 2,861	0.68	6,366 ± 2,111	6,556 ± 2,759	0.75
Average daily METs	1.8 ± 0.3	1.8 ± 0.3	0.99	1.9 ± 0.3	2.0 ± 0.5	0.36	1.8 ± 0.3	1.8 ± 0.2	0.77
Sedentary (min/day)	579 ± 56	569 ± 60	0.58	533 ± 50	511 ± 86	0.25	585 ± 61	583 ± 58	0.89
Moderate-intensity PA (min/day)	93 ± 55	96 ± 48	0.78	120 ± 78	127 ± 82	0.51	88 ± 29	82 ± 31	0.41
Habitual dietary intake									
Total energy (kcal)	2,406 ± 486	2,167 ± 560	0.06[a]	2,483 ± 563	2,445 ± 447	0.77	2,426 ± 381	2,383 ± 366	0.71
Carbohydrate (g)	283 ± 66	236 ± 80	0.02*	319 ± 107	306 ± 97	0.54	260 ± 47	244 ± 44	0.39
Fat (g)	93 ± 21	87 ± 20	0.39	95 ± 23	93 ± 22	0.82	98 ± 23	101 ± 20	0.76
Protein (g)	100 ± 20	100 ± 24	0.96	92 ± 30	99 ± 37	0.51	106 ± 16	112 ± 41	0.53

P represents change within each condition. * denotes significant difference $p<0.05$. [a] denotes trend towards significance.

CON= Control; MICT= Moderate-intensity continuous training; HIIT = High-intensity interval training; TEE = total energy expenditure; PAEE = Physical activity energy expenditure; METs = Metabolic equivalent of task.

Table 4. Body composition (mean ± SD).

	Control (n=9)			MICT (n=8)			HIIT (n=10)			Effect Sizes			
	Before	After	*P*	Before	After	*P*	Before	After	*P*	Interaction *P*	CON-MICT	CON-HIT	MICT-HIT
Total body composition													
Body weight (kg)	93.1 ± 11.8	94.0 ± 12.8	0.07[a]	96.7 ± 18.7	96.2 ± 17.8	0.39	96.0 ± 7.7	97.4 ± 7.9	0.002*	0.03*	0.09	0.05	0.14
Total fat mass (kg)	28.7 ± 8.7	28.9 ± 8.9	0.64	31.6 ± 10.2	31.3 ± 10.1	0.32	28.3 ± 5.3	28.9 ± 5.3	0.11[a]	0.19	0.05	0.06	0.11
Total fat-free mass (kg)	64.4 ± 6.1	65.1 ± 6.7	0.10[a]	65.0 ± 11.4	65.0 ± 10.3	0.90	67.7 ± 4.8	68.6 ± 4.6	0.02*	0.22	0.08	0.04	0.11
Total lean mass (kg)	61.1 ± 5.9	61.8 ± 6.5	0.11[a]	61.8 ± 11.0	61.8 ± 9.9	0.90	64.2 ± 4.9	65.1 ± 4.7	0.02*	0.23	0.08	0.04	0.11
Regional adiposity													
Trunk fat mass (kg)	16.3 ± 6.6	16.5 ± 6.8	0.51	18.0 ± 6.7	17.8 ± 6.2	0.40	16.2 ± 3.3	16.7 ± 3.4	0.08[a]	0.20	0.06	0.06	0.14
Android fat mass (kg)	2.87 ± 1.42	2.88 ± 1.41	0.80	3.31 ± 1.59	3.19 ± 1.44	0.09[a]	2.84 ± 0.70	2.94 ± 0.73	0.09[a]	0.06[a]	0.09	0.08	0.18
Gynoid fat mass (kg)	4.54 ± 1.04	4.56 ± 1.08	0.73	5.04 ± 1.36	4.92 ± 1.27	0.07[a]	4.28 ± 0.81	4.33 ± 0.73	0.35	0.13[a]	0.11	0.03	0.15
Visceral adipose tissue (cm^3)	1,384 ± 1,246	1,382 ± 1,176	0.97	1,409 ± 999	1398 ± 991	0.81	1,385 ± 467	1,473 ± 564	0.04*	0.21	0.01	0.1	0.13

P represents change within each condition unless indicated otherwise. * denotes significant difference $p<0.05$. [a] denotes trend towards significance.

CON=Control; MICT= Moderate-intensity continuous training; HIIT = High-intensity interval training.

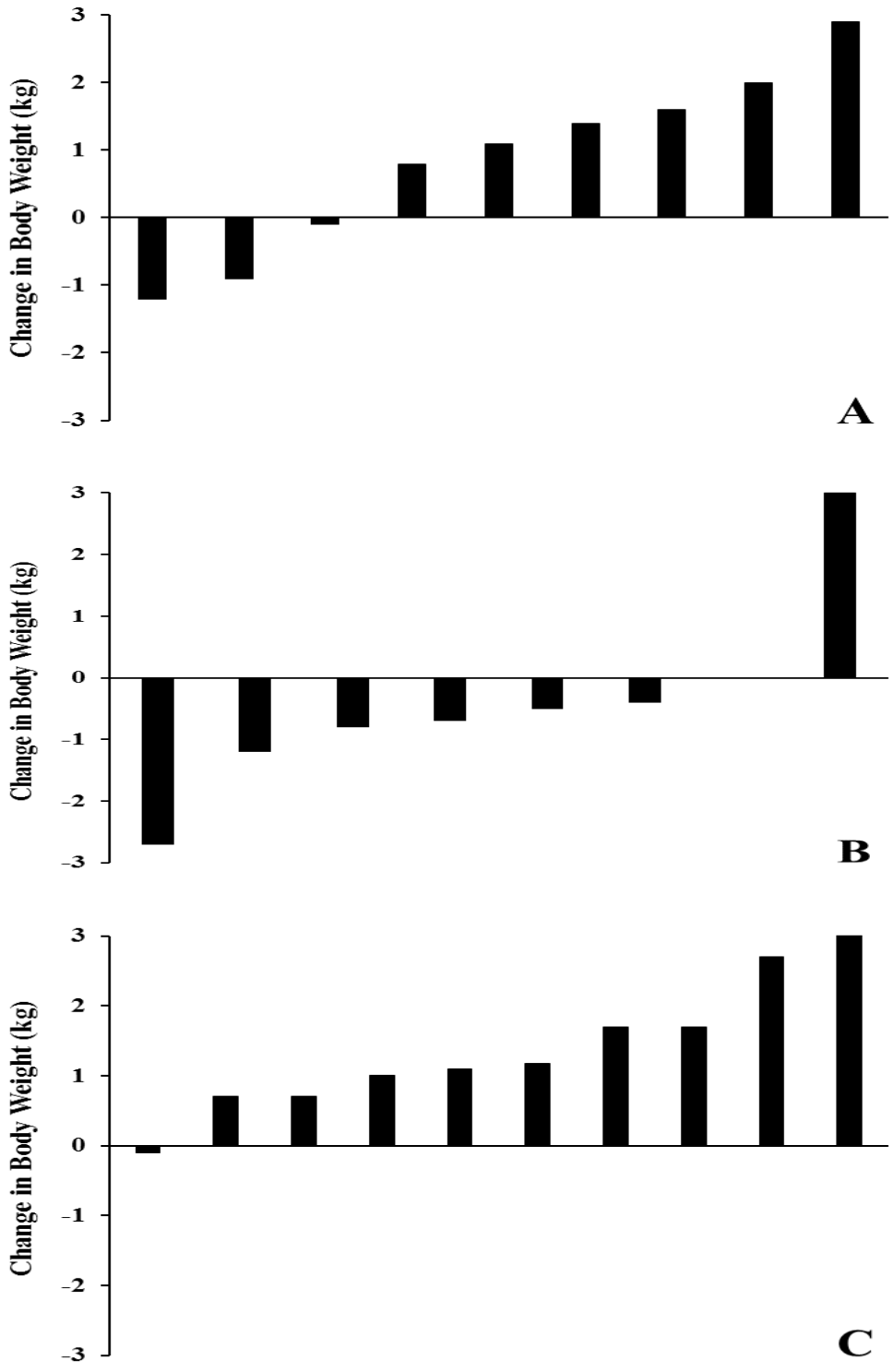

Figure 2. Individual changes in body weight (kg) during the intervention in A). Control, B). MICT and C). HIIT.

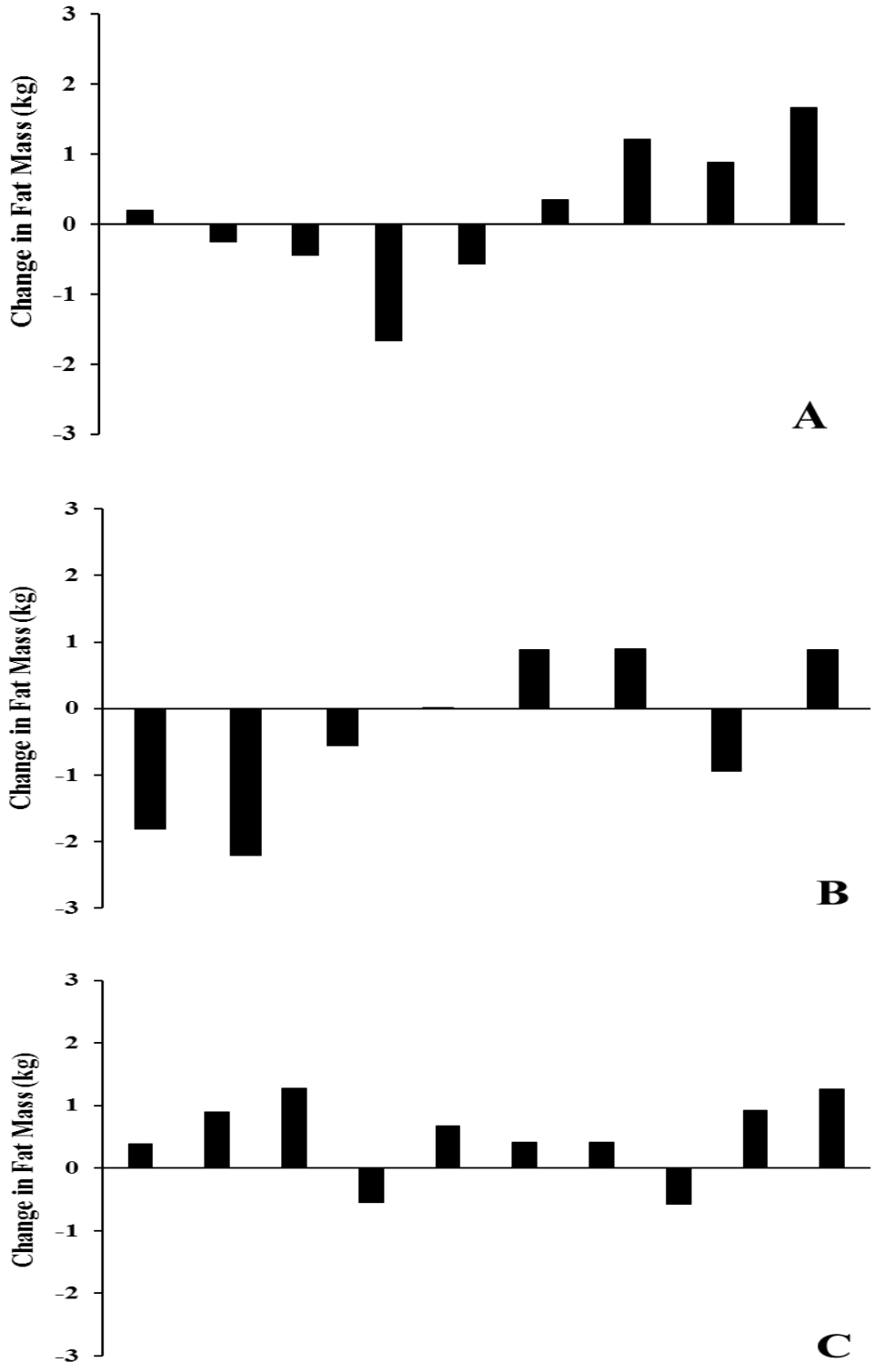

Figure 3. Individual changes in fat mass (kg) during the intervention in A) Control, B) MICT and C) HIIT. Order of subjects from left to right is same as in Figure 2.

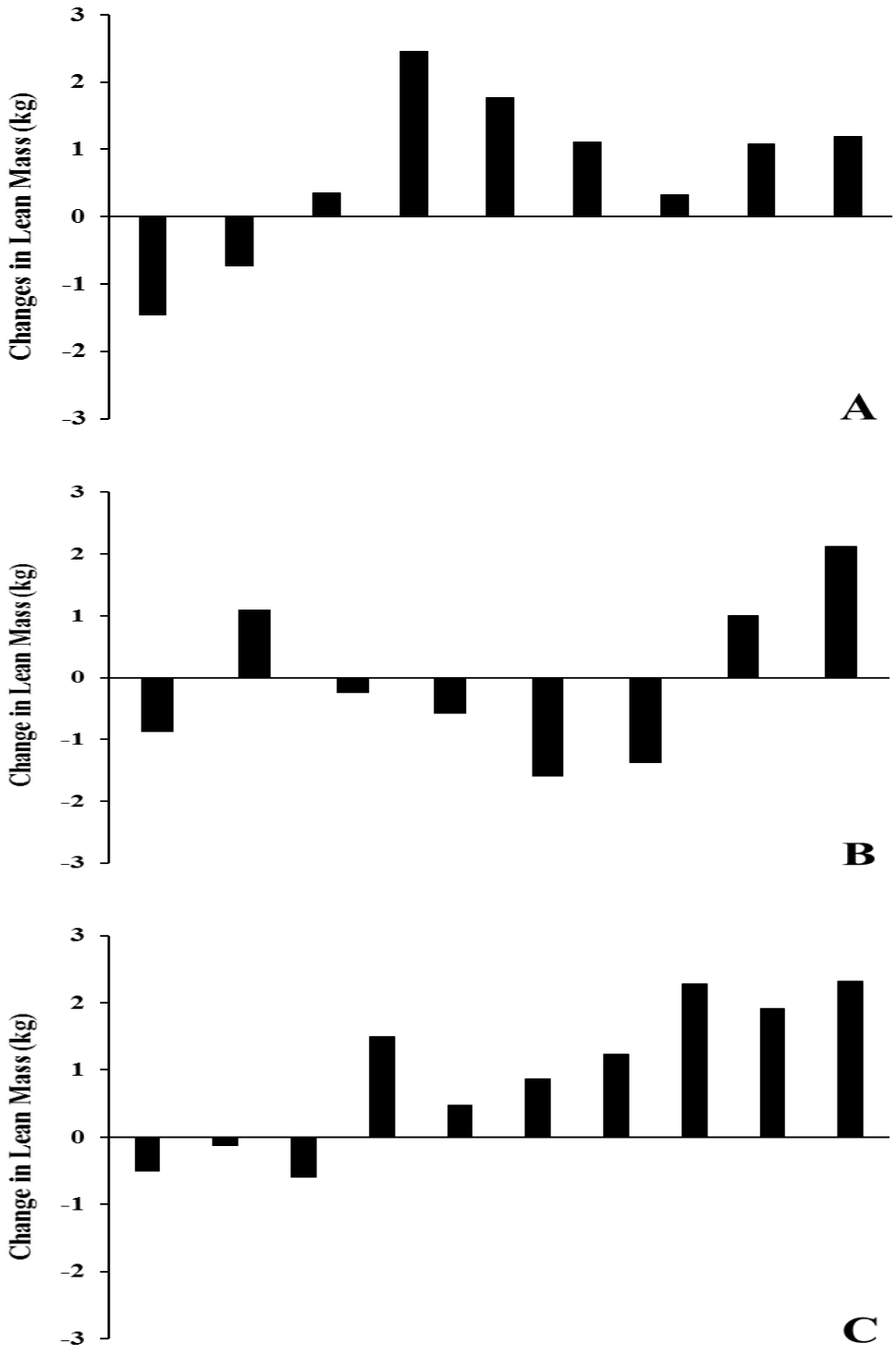

Figure 4. Individual changes in lean mass (kg) during the intervention in A) Control, B) MICT and C) HIIT. Order of subjects from left to right is same as in Figure 2.

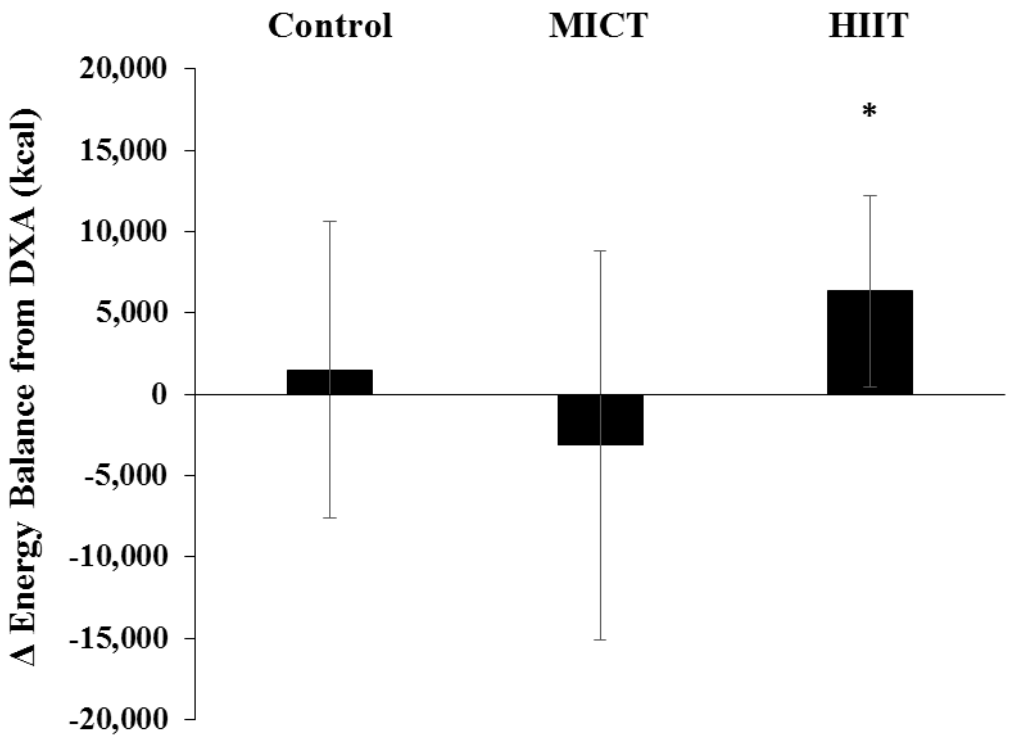

Figure 5. Actual changes in body energy balance (kcal) from DXA by condition. * denotes significant ($p < 0.05$) difference between MICT and HIIT.

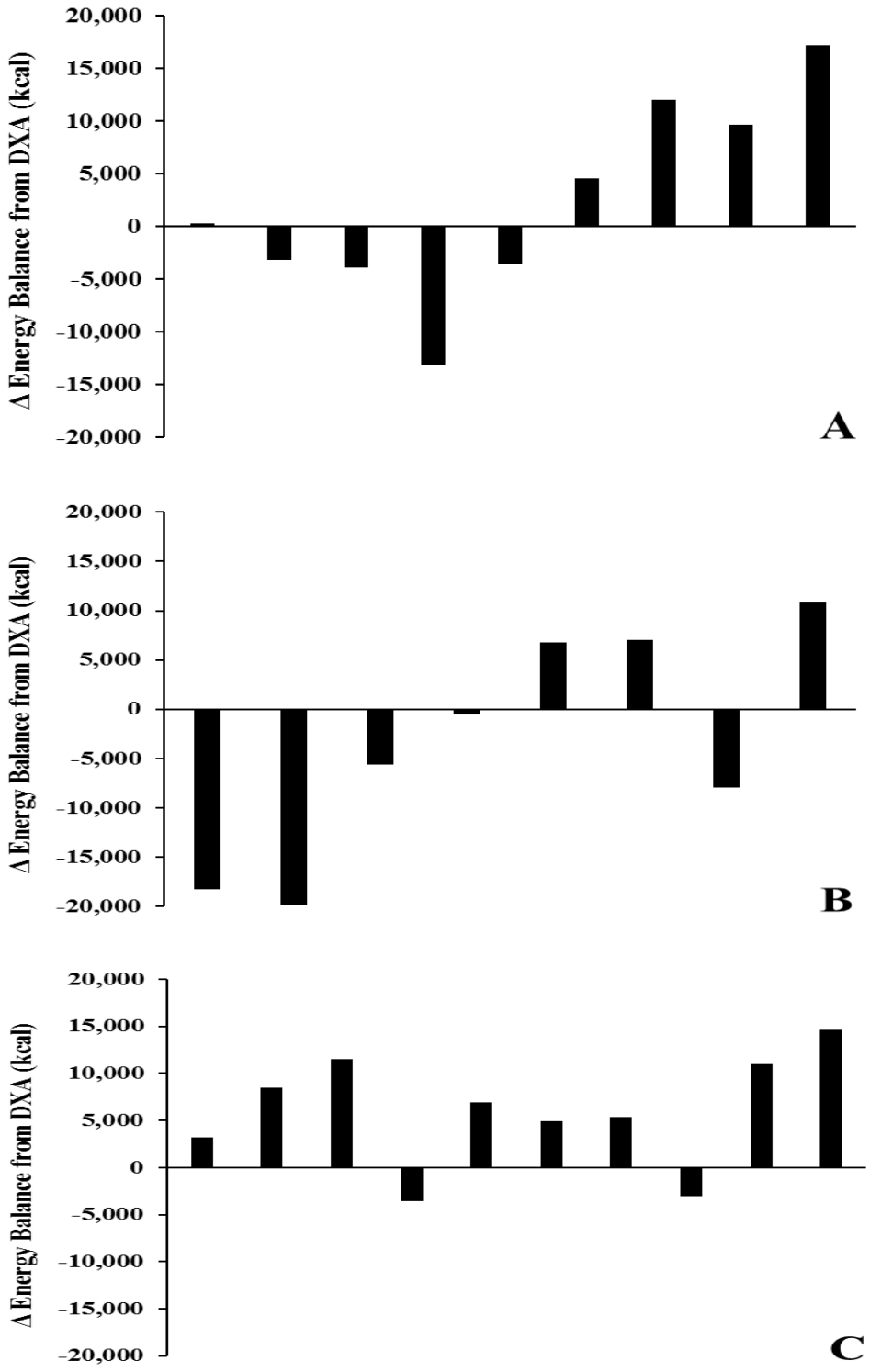

Figure 6. Individual changes in energy balance (kcal) from DXA in A) Control, B) MICT and C) HIIT. Order of subjects from left to right is same as in Figure 2.

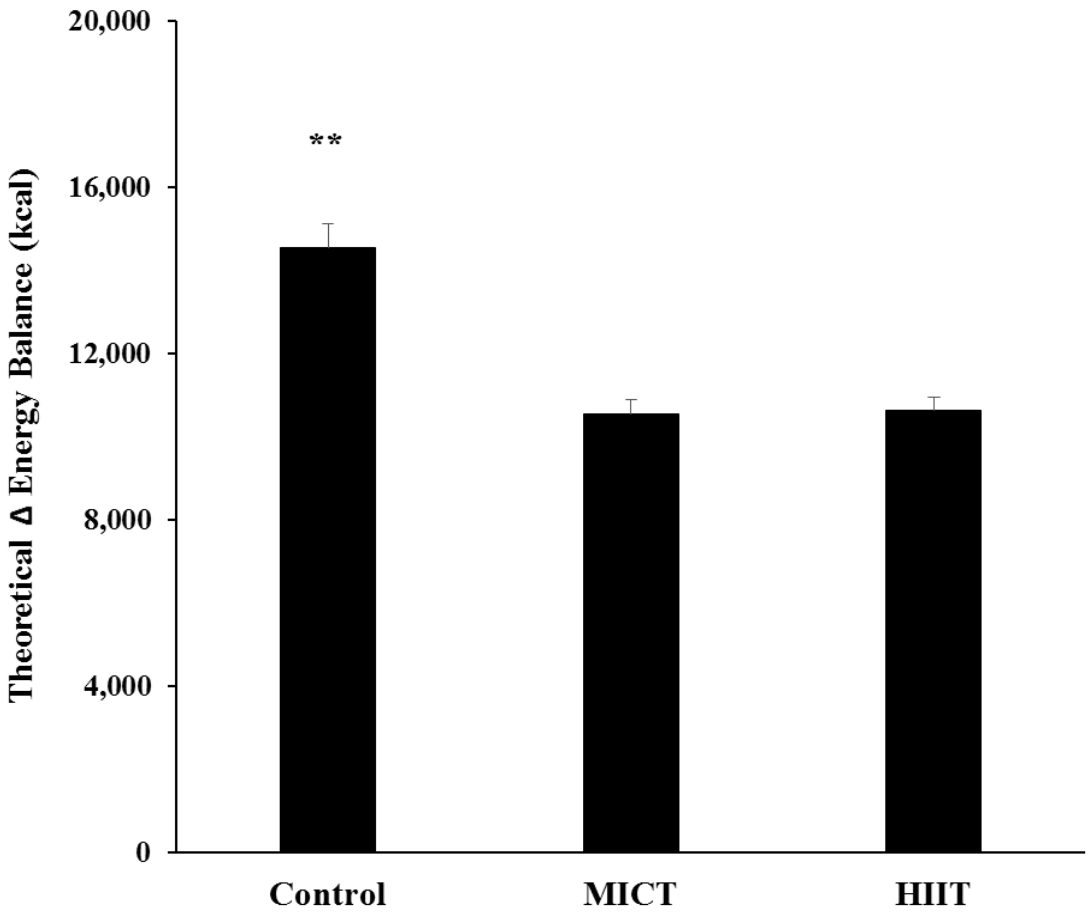

Figure 7. Theoretical change in energy balance (kcal). Calculated as excess energy intake minus exercise training during the intervention only across conditions. ** denotes significant $p<0.001$ time x condition interaction.

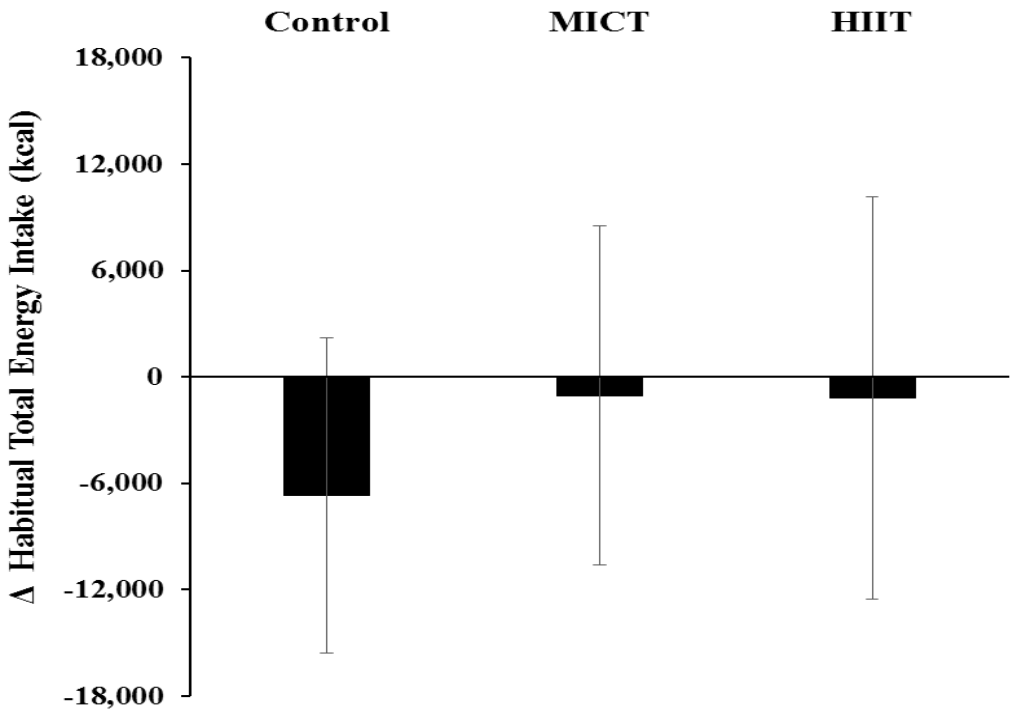

Figure 8. Changes in habitual energy intake (kcal) during the intervention by condition.

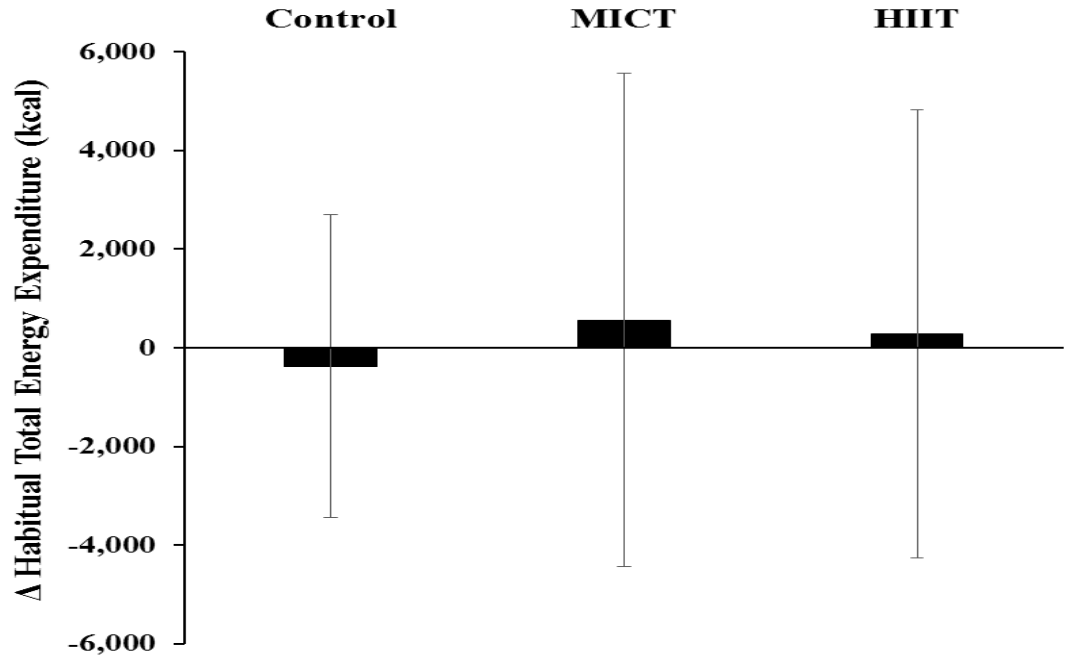

Figure 9. Changes in habitual energy expenditure (kcal) during the intervention by condition.

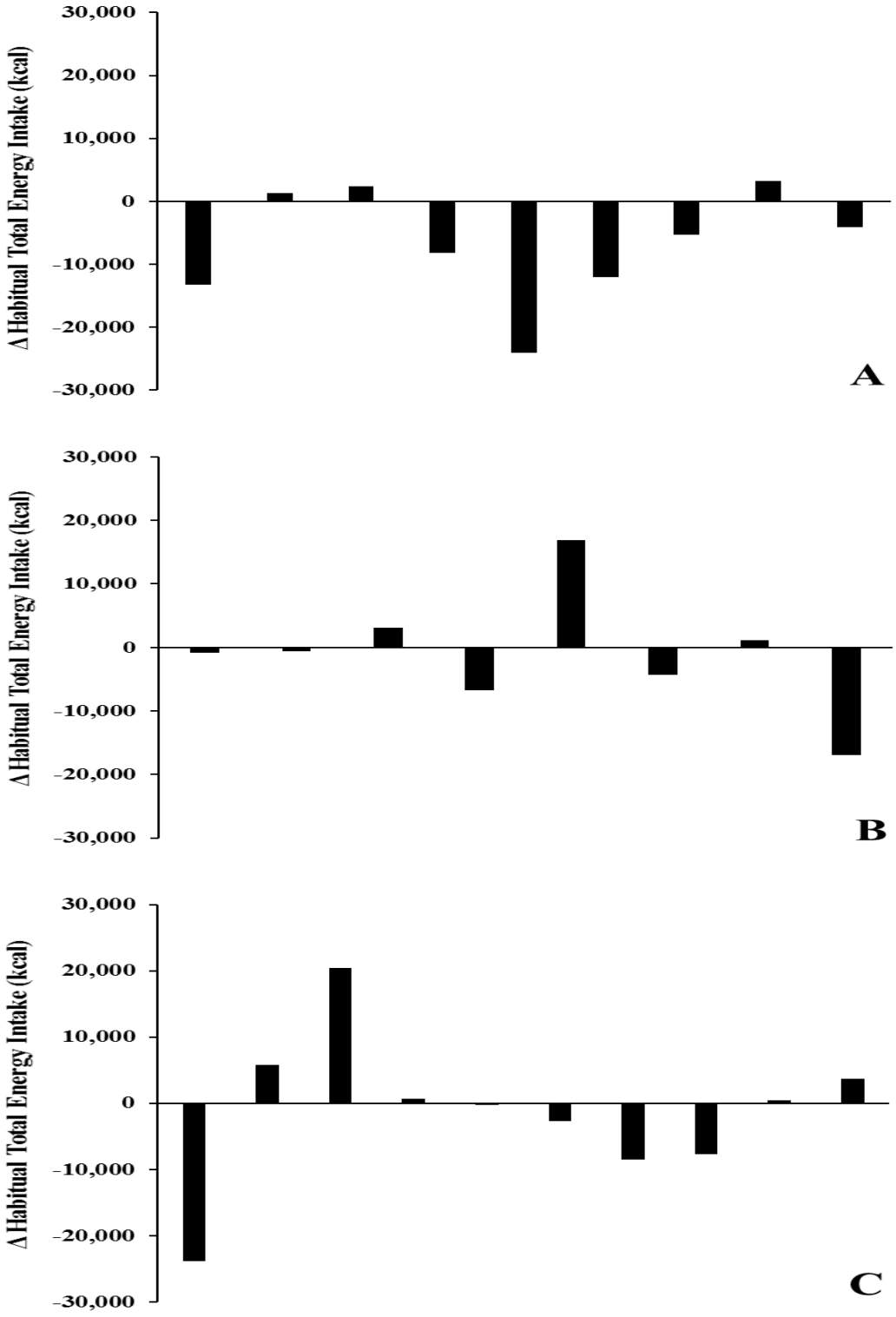

Figure 10. Individual changes in habitual energy intake (kcal) in A) Control, B) MICT and C) HIIT. Order of subjects from left to right is same as in Figure 2.

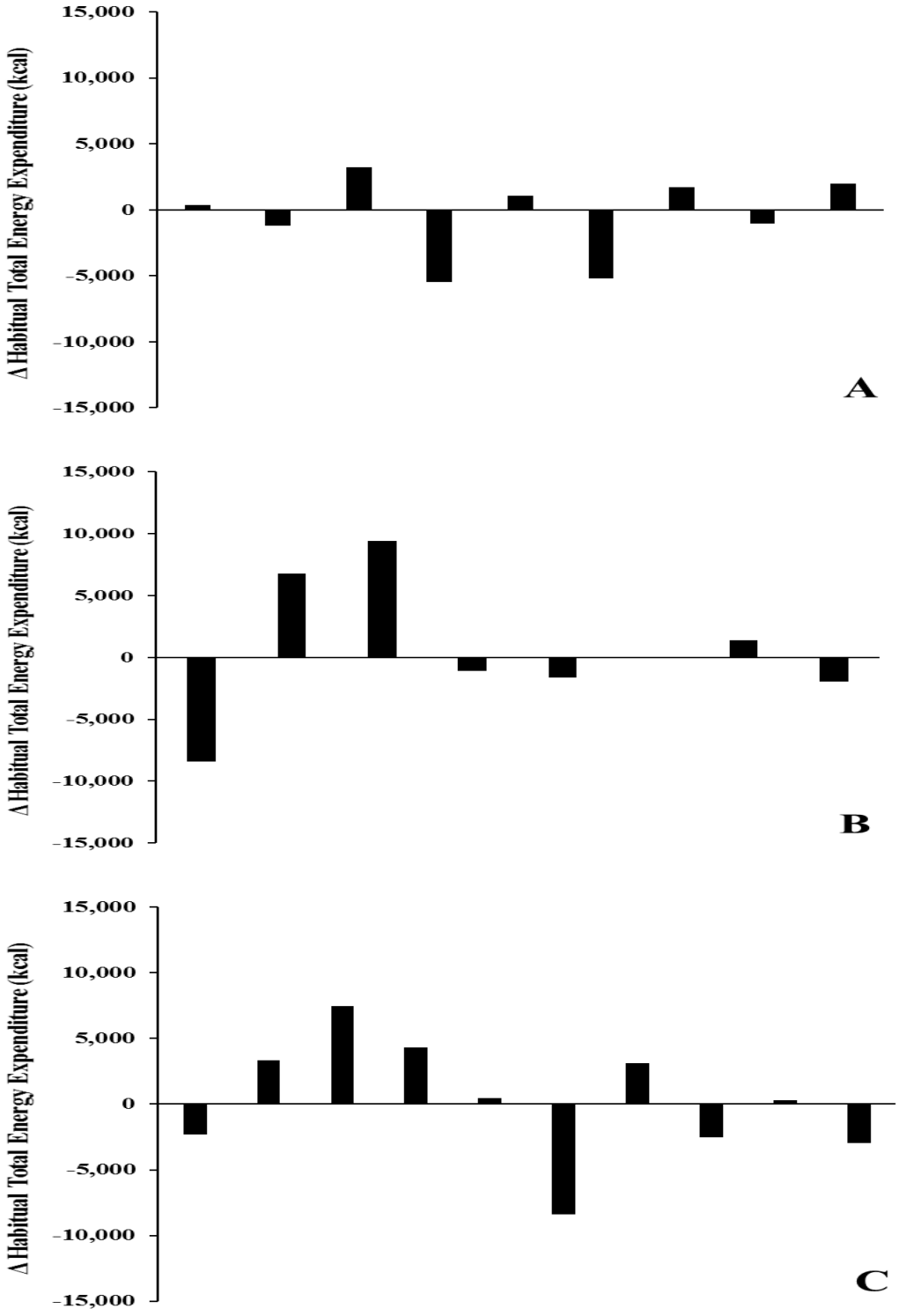

Figure 11. Individual changes in habitual energy expenditure (kcal) in A) Control, B) MICT and C) HIIT. Order of subjects from left to right is same as in Figure 2.

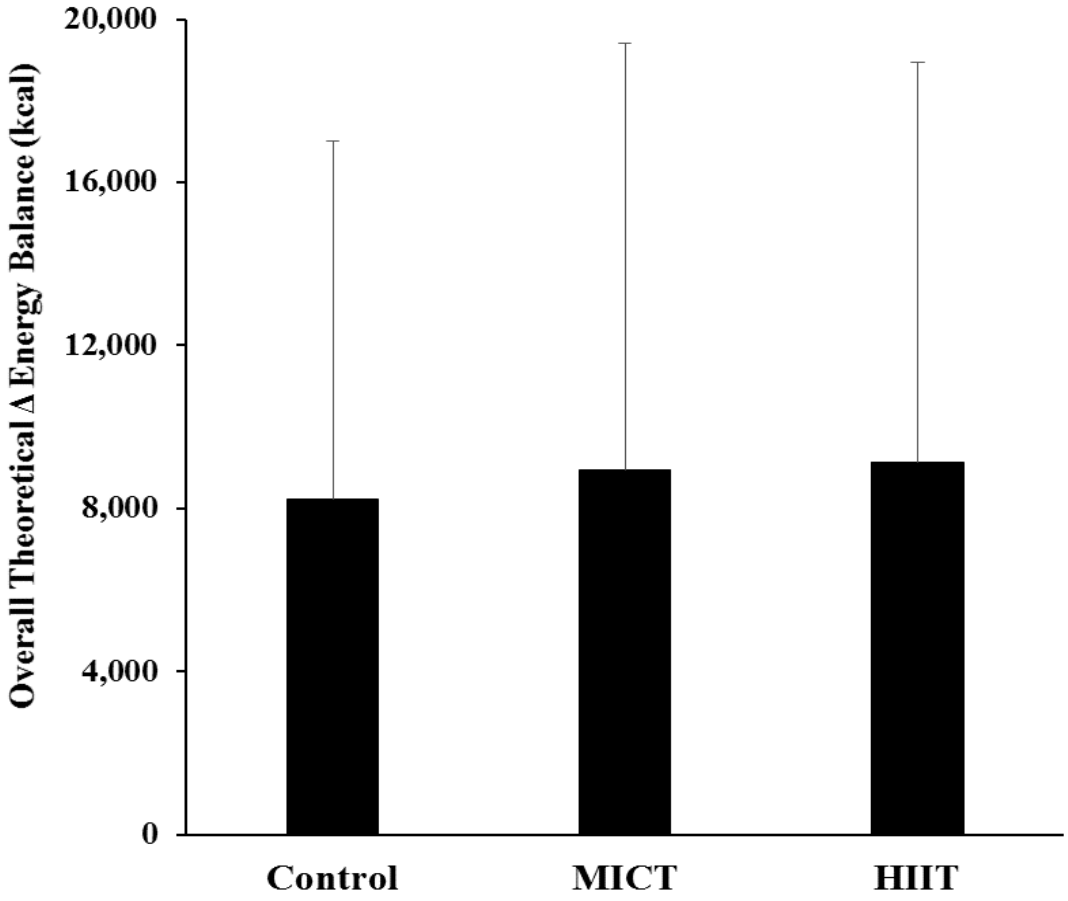

Figure 12. Overall theoretical predicted change in energy balance (kcal). Calculated as excess energy intake minus exercise training during the intervention plus changes in habitual energy intake minus changes in habitual energy expenditure across all conditions.

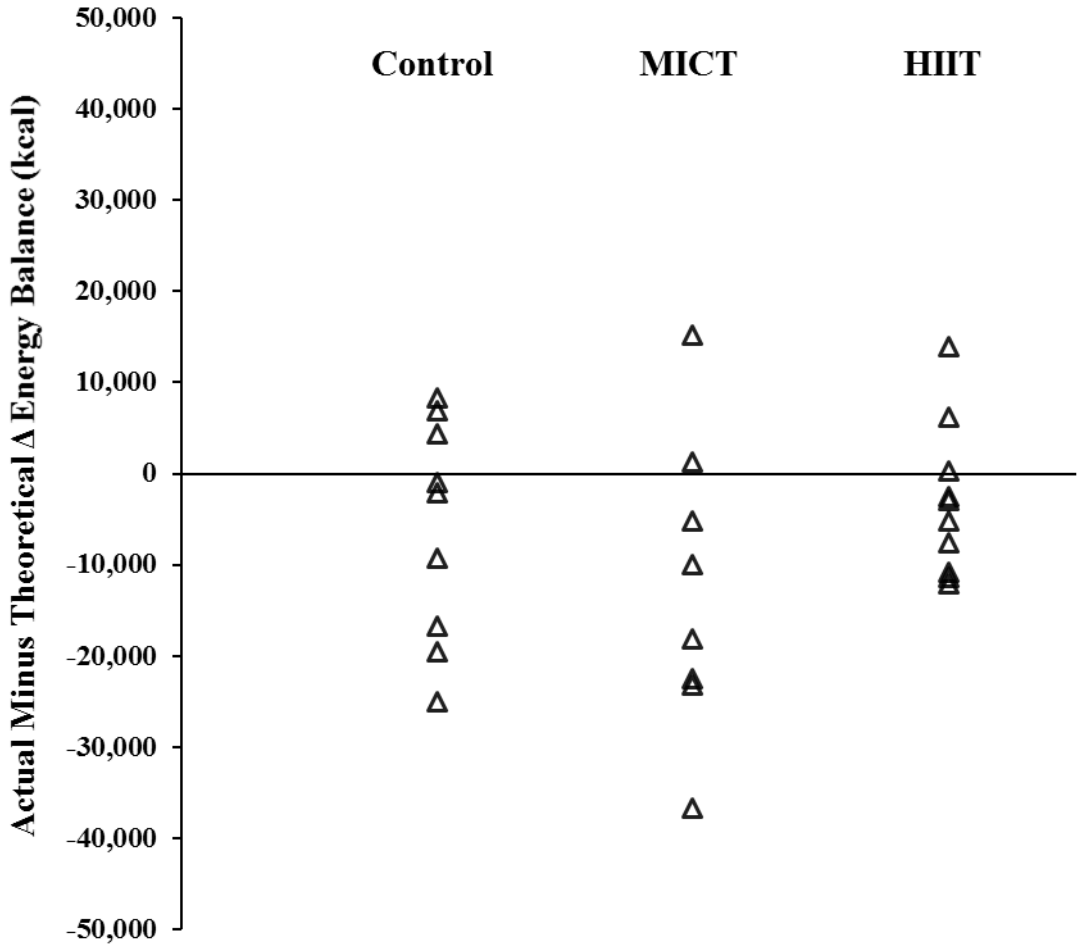

Figure 13. Energy compensation (kcal) in all subjects. Calculated as actual change in energy balance from DXA minus overall theoretical predicted change in energy balance across all conditions.

Blood Pressure, Arterial Stiffness and Endothelial Function

Peripheral SBP and DBP, and central SBP and DBP were unchanged in all groups (Table 5). For the arterial stiffness measures, there was a trend for time x group interaction in AP (p=0.12) and AIx@75 (p=0.11), with the HIIT group displaying a trend for reduction in AP (p=0.12) and AIx@75 (p=0.14) and the MICT group showing a trend for increase in AIx@75 (p=0.14) within group (Table 5). There was a trend (p=0.14) towards a significant reduction in cf-PWV after the intervention within the HIIT group, while control and MICT were unchanged.

For endothelial function, there was a trend towards a reduction in brachial artery FMD (p=0.16) and FMD normalized for shear (p=0.09) after the intervention in all groups (Figure 14 and 15, respectively). The magnitude of change was largest in the control group (Before: FMD 4.6 ± 1.2 %, After: FMD 3.7 ± 2.1 %; p=0.28) and smallest in the HIIT group (Before: FMD 6.0 ± 2.7%, After: FMD 5.5 ± 2.3%; p=0.56). However, there was no significant time x group interaction for FMD (p=0.92) or FMD normalized for shear (p=0.99). Baseline diameter, peak diameter, blood flow velocity and shear rate were unchanged within all groups (p: NS).

Table 5. Blood pressure and arterial stiffness (mean ± SD).

	Control (n=9)			MICT (n=8)			HIIT (n=10)			Effect Sizes			
	Before	After	*P*	Before	After	*P*	Before	After	*P*	Interaction *P*	CON-MICT	CON-HIT	MICT-HIT
Blood pressure													
Peripheral SBP (mmHg)	126 ± 9	128 ± 9	0.61	122 ± 9	125 ± 10	0.22	126 ± 9	125 ± 9	0.39	0.32	0.19	-0.31	-0.51
Peripheral DBP (mmHg)	76 ± 6	75 ± 9	0.38	73 ± 6	75 ± 9	0.35	75 ± 6	75 ± 9	0.88	0.44	0.61	0.33	0.28
Central aortic SBP (mmHg)	112 ± 8	113 ± 8	0.68	108 ± 8	111 ± 8	0.12[a]	112 ± 8	111 ± 8	0.42	0.24	0.27	-0.25	-0.52
Central aortic DBP (mmHg)	78 ± 6	76 ± 9	0.31	74 ± 6	76 ± 9	0.37	75 ± 6	76 ± 9	0.71	0.37	0.64	0.44	-0.20
Arterial stiffness													
Augmentation pressure (AP)	4.5 ± 3.6	5.2 ± 3.4	0.45	4.8 ± 3.6	6.1 ± 3.5	0.23	6.2 ± 3.6	4.8 ± 3.4	0.12[a]	0.12[a]	0.16	-0.57	-0.74
Augmentation Index (AIx) @ HR 75	5.5 ± 10.5	7.4 ± 10.7	0.46	7.3 ± 10.7	11.4 ± 10.9	0.14[a]	8.9 ± 10.6	5.3 ± 10.8	0.14[a]	0.11[a]	0.21	-0.51	-0.71
cf-Pulse wave velocity (PWV) (m/s)	6.8 ± 0.8	6.8 ± 0.8	0.84	6.9 ± 0.8	6.9 ± 0.8	0.66	6.7 ± 0.8	6.5 ± 0.8	0.14[a]	0.35	0.00	-0.25	-0.25

P represents change within each condition unless indicated otherwise. * denotes significant difference $p<0.05$. [a] denotes trend towards significance. Baseline moderate physical activity minutes included as a covariate in ANCOVA.

MICT= Moderate-intensity continuous training; HIIT = High-intensity interval training; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; cf = carotid-femoral.

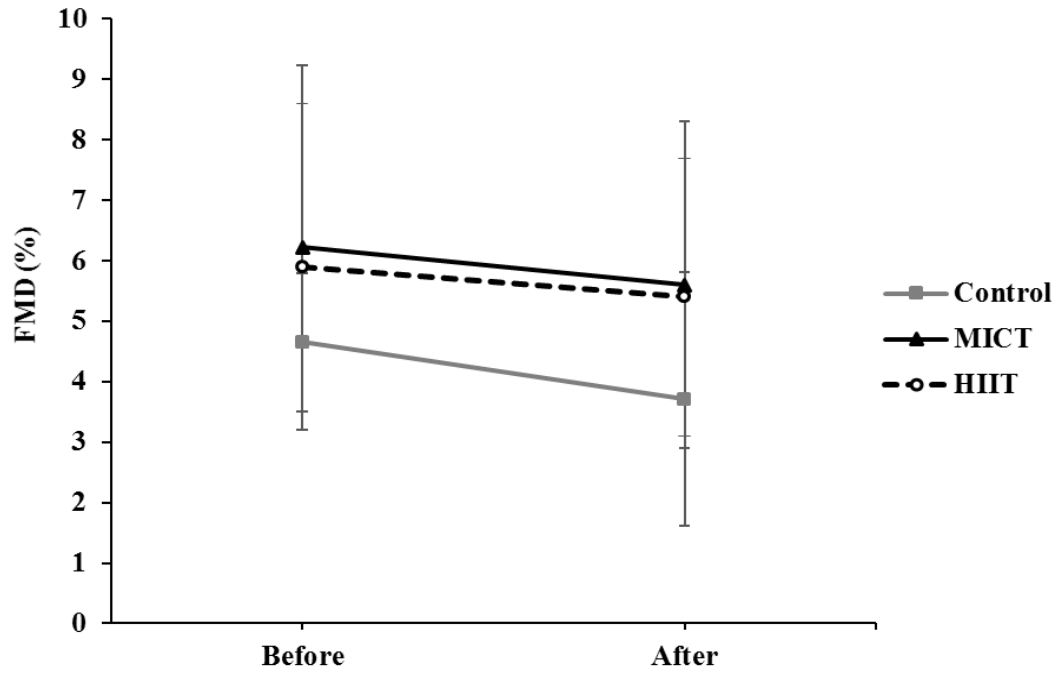

Figure 14. Changes in flow-mediated dilation (FMD %) by group.

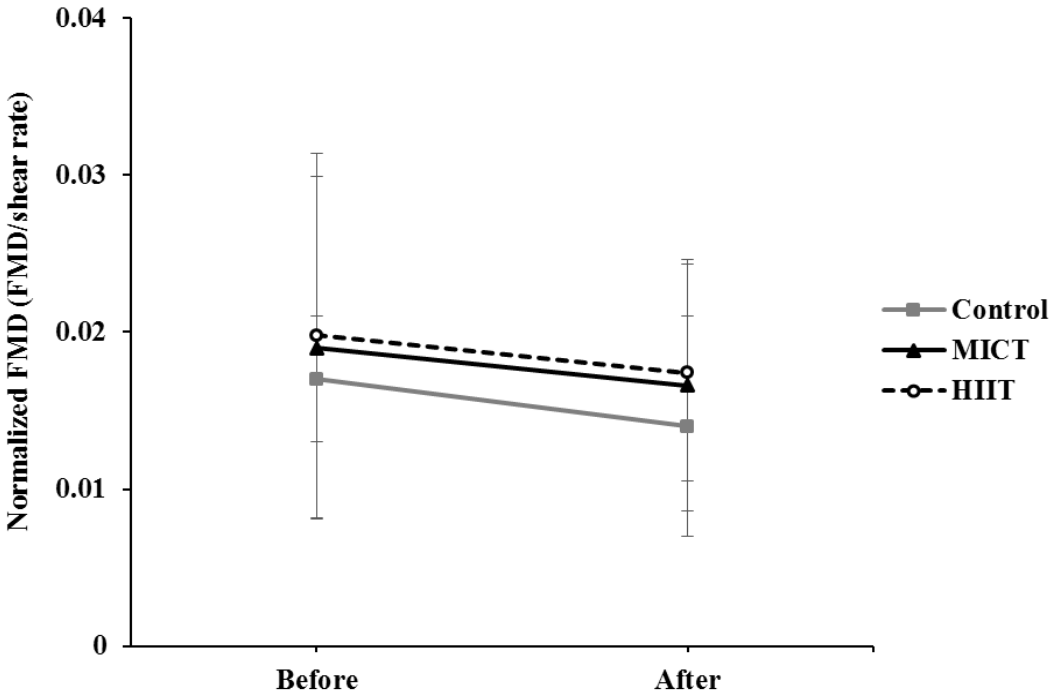

Figure 15. Changes in normalized flow-mediated dilation (FMD % /shear rate) by group.

Lipid and Glucose Metabolism

Results for blood lipid and glucose metabolism changes within group are presented in Table 6. There was a trend towards a reduction in triglycerides (p=0.10) in the HIIT group, and no significant change within MICT (p=0.74) and control (p=0.93). Total-, LDL- and HDL-cholesterol did not change significantly within all groups.

When comparing iAUC during the 2-h OGTT, there was a trend for a time x group interaction (p=0.07) with glucose significantly reduced within MICT (p=0.02) and control groups (p=0.002) and no significant change in the HIIT group (p=0.81). A closer examination of 2-h OGTT glucose curves revealed a significant condition x time interaction at 60 min (p=0.03) and a trend for condition x time at 90 min (p=0.16) (Figure 16). Within condition, there was a trend for reduction in glucose at 30 min in control (p=0.07) and MICT (p=0.17), and a significant reduction in glucose at 60 min (p=0.004 in control; p=0.007 in MICT) and 90 min (p=0.04 in control; p=0.04 in MICT) (Figure 16). Fasting and 120-min glucose were unchanged across all groups.

Insulin iAUC during the 2-OGTT was unchanged in all groups (Table 6). A closer examination of 2-h OGTT insulin curves revealed a significant time x condition interaction at 30 min (p=0.02), with a significant increase in insulin concentration at 30 min in control (p=0.04) and a significant reduction in insulin concentration at 30 min in MICT (p=0.03) (Figure 17). For hepatic IRI, there was a significant time x condition interaction (p=0.03) during the intervention, with a trend for an increase in hepatic IRI (p=0.07) in the control and a significant decrease in hepatic IRI (p=0.04) in the MICT group. Fasting insulin, HOMA-IR, IGI, DI and ISI did not change significantly within all groups (Table 6).

Table 6. Lipid and glucose metabolism (mean ± SD).

	Control (n=9)			MICT (n=7)			HIIT (n=10)			Effect Sizes			
	Before	After	*P*	Before	After	*P*	Before	After	*P*	Interaction *P*	CON -MICT	CON-HIT	MICT-HIT
Blood lipids													
Total cholesterol (mg/dl)	156 ± 25	156 ± 34	0.97	162 ± 27	155 ± 37	0.45	189 ± 26	183 ± 36	0.48	0.80	-0.27	-0.23	0.04
LDL cholesterol (mg/dl)	102 ± 27	104 ± 33	0.75	110 ± 29	104 ± 36	0.39	133 ± 28	131 ± 35	0.79	0.70	-0.28	-0.14	0.14
HDL cholesterol (mg/dl)	43 ± 8	45 ± 9	0.44	40 ± 9	42 ± 9	0.56	46 ± 8	45 ± 9	0.69	0.66	0.00	-0.37	-0.35
Triglycerides (mg/dl)	111 ± 40	111 ± 30	0.99	112 ± 43	114 ± 34	0.88	128 ± 42	105 ± 33	0.10[a]	0.37	0.05	-0.55	-0.58
Glucose and insulin indices													
Fasting glucose (mg/dl)	96 ± 6	94 ± 6	0.38	95 ± 6	94 ± 7	0.59	92 ± 6	91 ± 6	0.88	0.87	0.16	0.16	0.00
Glucose iAUC 0-120 (mg/dl*min)	5,612 ± 2,547	4,126 ± 2,229	0.002*	3,941 ± 2,685	2,742 ± 2,350	0.02*	3,329 ± 2,783	3,227 ± 2,438	0.81	0.07[a]	0.11	0.51	0.40
Fasting insulin (µU/ml)	13.0 ± 4.1	14.1 ± 4.9	0.28	11.2 ± 4.5	12.3 ± 5.1	0.34	12.0 ± 4.3	11.1 ± 4.9	0.34	0.27	0.00	-0.47	-0.45
Insulin iAUC 0-120 (µU/ml*min)	11,543 ± 5,331	11,682 ± 5,379	0.87	9,034 ± 5,827	7,904 ± 5,880	0.26	7,063 ± 5,619	7,082 ± 5,670	0.98	0.56	-0.22	-0.02	0.20
HOMA-IR	3.1 ± 1.0	3.3 ± 1.2	0.36	2.7 ± 1.1	2.9 ± 1.3	0.44	2.7 ± 1.1	2.5 ± 1.3	0.39	0.37	0.00	-0.37	-0.37
Hepatic Insulin Resistance Index (IRI)	8.1 ± 3.6	9.7 ± 4.9	0.07[a]	7.3 ± 4.0	5.2 ± 5.3	0.04*	5.6 ± 3.8	5.2 ± 5.2	0.67	0.03*	-0.96	-0.53	0.45
Insulinogenic Index (IGI)	1.5 ± 3.2	2.2 ± 1.9	0.23	3.5 ± 3.5	2.8 ± 2.0	0.30	2.4 ± 3.4	1.8 ± 2.0	0.39	0.22	-0.41	-0.39	0.03
Disposition Index (DI)	4.4 ± 9.0	6.8 ± 6.5	0.30	9.3 ± 9.9	10.2 ± 7.1	0.73	8.0 ± 9.5	6.8 ± 6.9	0.61	0.53	0.15	-0.38	-0.21
Matsuda Index	3.0 ± 1.7	3.1 ± 1.4	0.88	3.8 ± 1.9	4.2 ± 1.5	0.32	3.9 ± 1.8	3.7 ± 1.5	0.67	0.59	0.16	-0.17	-0.32

P represents change within each condition unless indicated otherwise. * denotes significant difference $p<0.05$. a denotes trend towards significance. Baseline moderate physical activity minutes included as a covariate in ANCOVA.

MICT= Moderate-intensity continuous training; HIIT = High-intensity interval training; LDL= Low-density lipoprotein; HDL = High-density lipoprotein; iAUC = Incremental area under the curve; HOMA-IR= Homeostatic model assessment of insulin resistance.

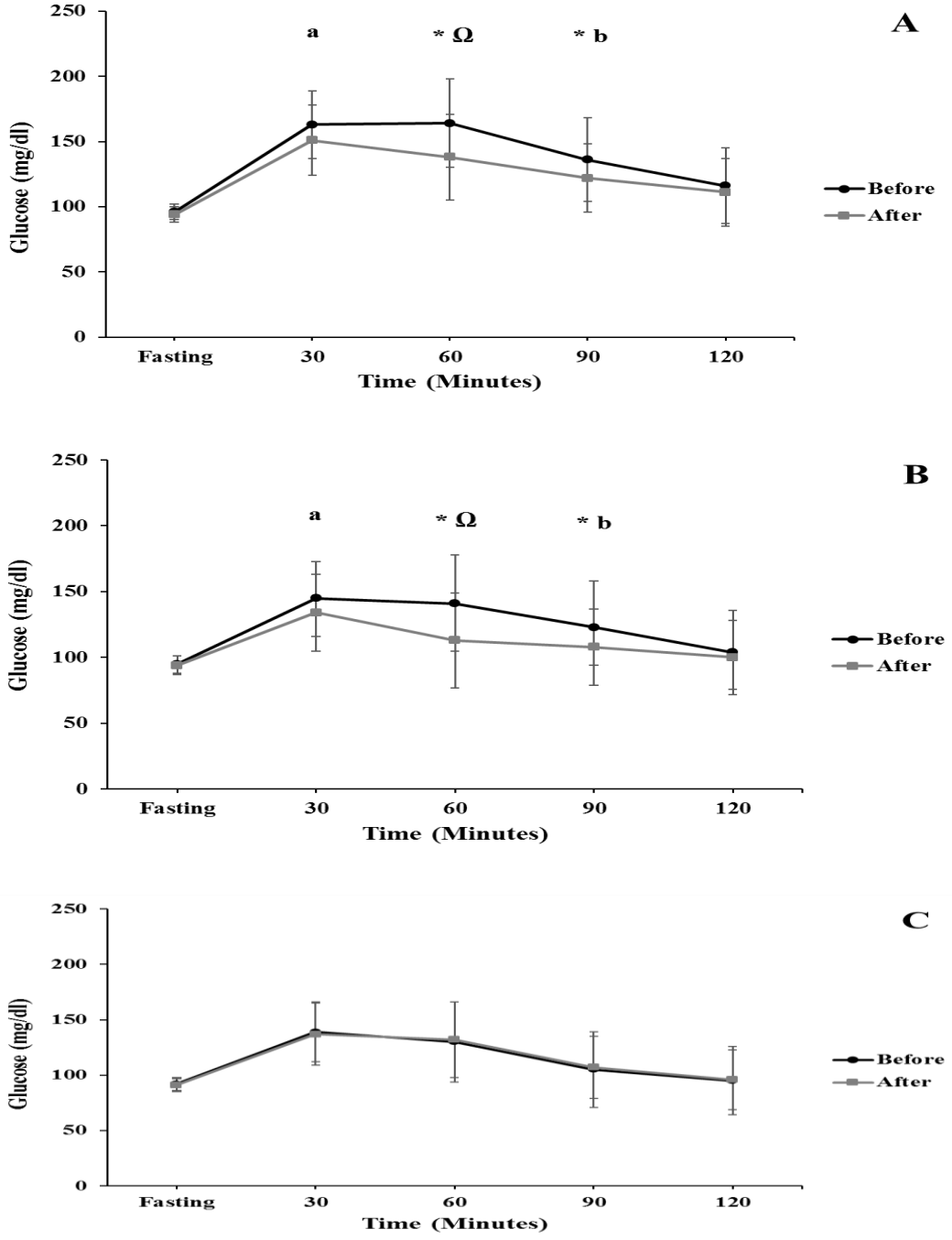

Figure 16. Glucose response to OGTT in A) Control, B) MICT and C) HIIT. * denotes significant ($p<0.05$) difference within condition. Ω denotes significant time x condition interaction ($p<0.05$). [a] denotes trend towards significant ($p<0.20$) difference within condition. [b] denotes trend towards significant ($p<0.20$) time x condition interaction.

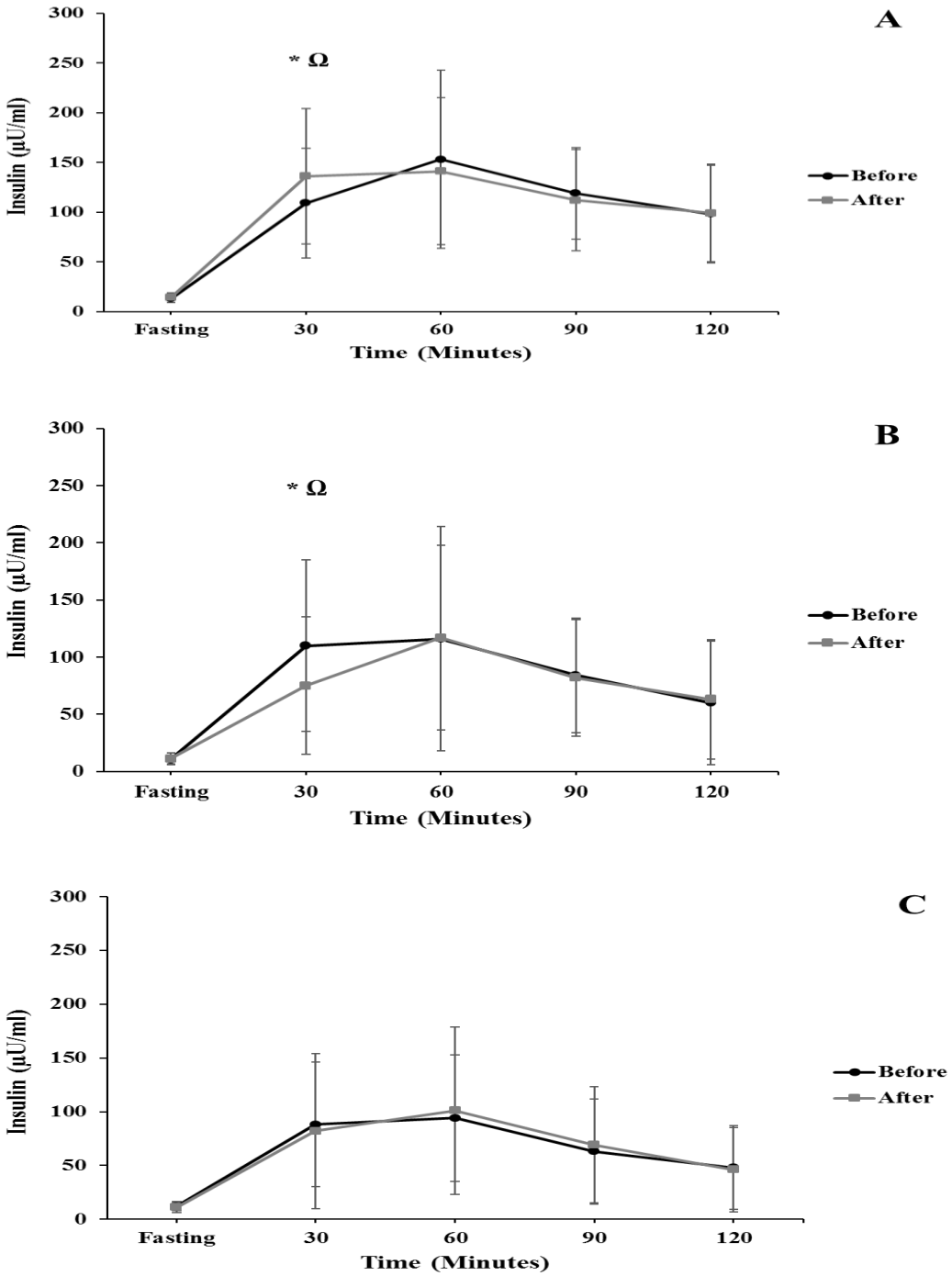

Figure 17. Insulin response to OGTT in A) Control, B) MICT and C) HIIT. * denotes significant ($p<0.05$) difference within condition. Ω denotes significant time x condition interaction ($p<0.05$).

Exercise Training and Cardiorespiratory Fitness

Total exercise time (including 10 min for warmup and cooldown) in the MICT group (37 ± 6 min) was significantly higher than the HIIT group (28 ± 2 min). Subjects in HIIT group performed an average of 10 ± 1 high-intensity intervals per session (range: 8-12 intervals). There was no significant difference in physical activity enjoyment scale (PACES) between MICT (104 ± 14) and HIIT (102 ± 20) ($p = 0.78$).

There was a significant time x group interaction for VO_{2peak} ($p<0.001$) (Figure 18 and Table 7). Absolute (L/min) and relative (ml/kg/min) VO_{2peak} increased significantly in the MICT and HIIT groups ($p<0.001$ within condition for both absolute and relative VO_{2peak}), while the control group did not change ($p = 0.88$ and $p=0.91$, respectively). There was also a significant time x group interaction for time to exhaustion (TTE) and maximal power output (MPO) ($p<0.001$) (Table 7). There was a significant increase within both MICT and HIIT for TTE and MPO ($p<0.001$) and a trend towards a significant reduction in the control group ($p=0.05$).

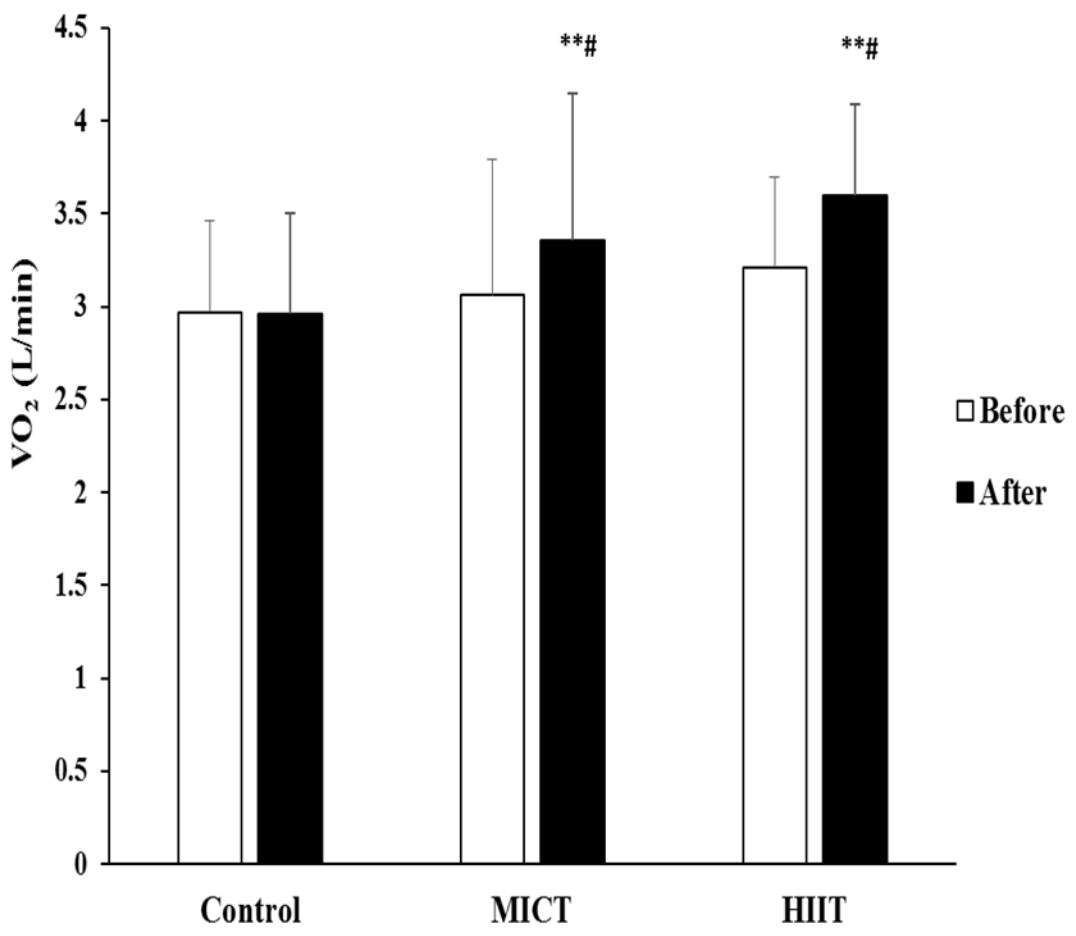

Figure 18. Changes in peak oxygen uptake (VO_{2peak}) by condition. ** denotes significant $p<0.001$ before vs. after within group. # denotes significant $p<0.001$ time x group interaction.

Table 7. Cardiorespiratory fitness (mean ± SD).

	Control (n=9)			MICT (n=8)			HIIT (n=10)			Effect Sizes			
	Before	After	*P*	Before	After	*P*	Before	After	P-value	Interaction *P*	CON -MICT	CON-HIT	MICT-HIT
Cardiorespiratory fitness													
VO_{2peak} (L/min)	2.97 ± 0.49	2.96 ± 0.54	0.88	3.06 ± 0.73	3.36 ± 0.79	p<0.001*	3.21 ± 0.49	3.60 ± 0.49	p<0.001*	p<0.001*	0.50	0.80	0.15
VO_{2peak} (ml/kg/min)	31.9 ± 4.3	31.7 ± 4.8	0.81	31.5 ± 5.2	34.8 ± 5.6	p<0.001*	33.7 ± 6.4	37.4 ± 6.3	p<0.001*	p<0.001*	0.71	0.69	0.07
Time to exhaustion (sec)	410 ± 80	395 ± 89	0.05[a]	390 ± 92	425 ± 94	p<0.001*	438 ± 63	507 ± 59	p<0.001*	p<0.001*	0.57	1.16	0.43
Maximal power output (Watts)	247 ± 41	240 ± 44	0.05[a]	235 ± 49	254 ± 48	p<0.001*	260 ± 30	295 ± 30	p<0.001*	p<0.001*	0.57	1.16	0.40

P represents change within each condition unless indicated otherwise. * denotes significant difference p<0.05. [a] denotes trend towards significance.

MICT= Moderate-intensity continuous training; HIIT = High-intensity interval training; VO_{2peak}= Peak Oxygen Uptake.

CHAPTER 5

DISCUSSION

In this study, exercise training 4 days a week with MICT or HIIT was utilized to examine the efficacy of exercise to prevent the expected deleterious effects of a fat-sugar supplemented diet on body composition, glycemic control, vascular function and other blood markers of cardiovascular risk in an at-risk population of overweight and obese, sedentary males. After four weeks of sustained overfeeding by approximately 606 kcal per day in the form of donuts, it was found that exercise training (regardless of intensity) was not superior to the control condition for preventing weight gain and deleterious changes in most of the cardiometabolic risk markers. A major reason for the null findings can be attributed to the fact that the control group (donut supplement only) did not demonstrate any negative health effects after the intervention.

It was hypothesized that the intake of 4 dozen donuts (+14,554 kcal) over 4 weeks would negatively impact body composition in terms of weight and fat gain and that exercise training (MICT or HIIT) would prevent this deleterious outcome. In addition, it was hypothesized that HIIT would yield more favorable changes in body composition as compared to MICT. The results of the study do not support these hypotheses, with body weight increasing significantly in HIIT and trending towards a significant increase in control. The MICT group was unchanged and superior to HIIT for preventing weight gain. Fat mass was unchanged across all conditions. In contrast, lean mass increased significantly in HIIT and trended toward a significant increase in control, while remaining unchanged in the MICT group. This finding is similar to Walhin et al. (2013) who showed that 7 days of overfeeding (+1,500 kcal/day) plus step reduction (<4,000

steps) yielded significant increases in lean mass (~96% of increase in overall body weight) and little change in fat mass. Furthermore, the addition of daily exercise in the form of 45 min of treadmill running during this period of overfeeding increased lean mass (~63% of increase in overall body weight) and fat mass. In contrast, others studies have shown that periods of overfeeding and inactivity (14 days) yield large increases in fat mass (~98% of increase in overall body weight) with little change in lean mass (Knudsen et al., 2012; Krogh-Madsen et al., 2014). The differences in these findings may be attributable to differences in study duration. It is common to observe significant increases in lean mass during the 1st seven days of overfeeding due to increased glycogen storage (Horton et al., 1995), which would explain the large increase in lean mass observed after 7 days of overfeeding. It should be highlighted that previous overfeeding studies chose to reduce step counts by 70-85% in the control conditions (Knudsen et al., 2012; Krogh-Madsen et al., 2014; Walhin et al., 2013). In contrast, when regular step counts were maintained during periods of overfeeding the accumulation of body fat (+0.6 kg) was less than a reduced step count control (+1.4 kg) (Krogh-Madsen et al., 2014). The control group in my study did not change step counts or physical activity levels during the intervention, which may in part explain why I did not observe the same deleterious effects in body composition and cardiometabolic risk factors as previously reported by others (Knudsen et al., 2012; Krogh-Madsen et al., 2014; Walhin et al., 2013).

Based on the intervention alone, the donuts should have theoretically yielded a 14,554 kcal positive energy balance in the control, which is greater than the two exercise conditions (+10,550 kcal) (Figure 7). However, the actual changes in energy balance (as

reflected by DXA) reveal a much smaller change (+2,228 kcal) in the control group (Figure 5). A potential explanation for the lack of significant findings for body composition and other cardiometabolic risk factors may in part be due to a compensatory down-regulation of habitual energy intake in the control group (an estimated −6,681 kcal over 4 weeks) which was not observed in the exercise conditions during the intervention (Figure 8). Carbohydrate was the only macronutrient that decreased significantly in the control group, with a 28% reduction in habitual dietary intake of sugar (Pre: 104 g/day, Post: 75 g/day) during the intervention. All subjects were instructed to keep their diet constant and add the donuts as snacks between meals on 6 days per week to induce a +606 kcal/day positive energy balance. However, the reduction in the sugar intake (−29 g/day) in the control group suggests that sugary snacks present in the diet at baseline may have been directly replaced with donuts (+30 g/day of sugar), resulting in a decrease in habitual energy and sugar intake during the intervention. However, it should be pointed out that reduction in habitual dietary intake explains only ~55% of the difference between theoretical and actual energy balance (+12,326 kcal) in the control.

The Harris-Benedict equation (J. A. Harris & Benedict, 1918) estimated the daily energy intake needed to maintain body weight in our subjects as ~3,000 kcal/day. However, habitual energy intake calculated from food records is only ~2,400 kcal/day (Table 3). This suggests that the subjects in the current study may have underestimated their daily energy intake by as much 25%. Systematic underreporting of caloric intake through self-report measures is not uncommon, particularly in those who are overweight or obese (Dhurandhar et al., 2015; Lichtman et al., 1992; Schoeller, Bandini, & Dietz, 1990). Lichtman et al. (1992) previously reported that obese subjects underreport energy

intake by as much as 47%. Similarly, Schoeller et al. (1990) demonstrated that self-report measures of dietary intake systematically underestimate energy intake by hundreds of kcal/day and obese individuals underreport intake by as much 50% when compared to doubly labeled water. Thus it is possible that the magnitude of compensation related to habitual energy intake during the intervention may have been even larger than the −6,681 kcal estimated by food records during the intervention.

Another potential explanation for the disparity between actual and predicted changes in energy balance in the control group could be changes in habitual physical activity during the intervention. However, objective assessment of step counts and energy expenditure before and during the final week of the intervention revealed no changes in habitual physical activity across all conditions. The physical activity monitor used in this study (SenseWear Armband) has been shown to systematically overestimate total energy expenditure and moderate physical activity minutes (Bhammar, Sawyer, Tucker, Lee, & Gaesser, 2016). However, its reliability for tracking changes in physical activity between different time points is excellent (Bhammar et al., 2016; Tucker, Bhammar et al., 2015). Furthermore, VO_{2peak} did not change in the control group, reinforcing our accelerometer findings that physical activity levels did not change during the intervention.

Another plausible explanation for the large differences between actual and predicted changes in energy balance observed during this intervention (Figure 13) may be related to increases in resting metabolic rate (RMR) associated with high energy intake (Tremblay, Despres, Theriault, Fournier, & Bouchard, 1992). Although we did not directly measure changes in RMR in this study, it has previously been reported that periods of overfeeding (+84,000 kcal over 100 days) can result in a ~10% elevation in

daily RMR (Tremblay et al., 1992). In fact, a recent study by Walhin et al. (2013) demonstrated an 11% increase in daily RMR after just 7 days of overfeeding (+50% kcal/day over habitual diet) in young men. The daily energy surplus in the current study was not as high as the aforementioned studies but even a 5% increase in daily RMR could yield a compensation of 3,000 calories or more. Furthermore, our study is not the first to notice large differences between energy intake and actual changes in body energy balance as assessed by DXA. Walhin et al. (2013) overfed individuals by 11,327 kcal over 7 days and only witnessed an actual change in energy balance from DXA of 3,814 kcal and 6,824 kcal in control and exercise groups, respectively. Similarly, Krogh-Madsen et al. (2014) overfed individuals by ~29,000 kcal over 14 days and only observed an actual change in energy balance from DXA of 13,136 kcal. Furthermore, periods of excess dietary intake typically yield large individual differences in body composition changes (Black, 2013; Stevenson et al., 2013; Yanovski et al., 2000).

I observed large individual variability for changes in body composition and energy balance in this study with some subjects gaining as much as 3.7 kg (~ +17,241 kcal in body energy balance) and others losing 2.7 kg (~ -19,884 kcal in body energy balance). These observations are similar to Black (2013) who observed large individual differences in changes in fat mass during a period of fat-sugar overfeeding with some individuals gaining ~3.5 kg of fat and others losing ~2.2 kg of fat in just 3 weeks of a donut-supplemented diet the same as that used in the present study. Similarly, an observational study assessing changes in body weight during the winter holiday period reported changes in body weight ranging from ─2.3 to +6.3 kg during a 5 week period (Stevenson et al., 2013). A seminal overfeeding study conducted in 12 pairs of

monozygotic twins showed that 100 days of overfeeding (+84,000 kcal) yielded large individual differences between twin pairs for body weight and fat deposition, with a range of 4.3 to 13.3 kg range in weight gain (Bouchard et al., 1990). Large individual differences in body composition changes have also been reported in aerobic exercise training studies (Donnelly et al., 2003; King et al., 2009; Sawyer, Bhammar et al., 2015). It has been suggested that individual differences in weight gain may in part be explained by differences in metabolic flexibility (Horton et al., 1995). Therefore, identifying individuals who are at-risk for weight gain during periods of excess intake such as the winter holidays may be a suitable treatment strategy for obesity.

The results for changes in regional adiposity do not support my hypothesis that both exercise conditions (MICT or HIIT) would induce superior beneficial changes relative to control. In contrast, visceral adipose tissue increased significantly in HIIT and was unchanged in MICT and control. It has previously been documented that high amounts of visceral adipose tissue increase the risk of hypertension, dyslipidemia and diabetes (Jensen, 1997). Furthermore, increases in visceral and abdominal adiposity during overfeeding has been shown to be strongly correlated with increased arterial stiffness in as little as 6-8 weeks (Orr et al., 2008) and insulin resistance (Knudsen et al., 2012; Krogh-Madsen et al., 2014). Interestingly, we did not observe any deleterious changes in arterial stiffness, blood pressure, or any insulin resistance indices despite a significant increase in visceral adipose tissue in the HIIT condition. In contrast, we observed trends toward improvement in the augmentation pressure, augmentation index and carotid-pulse wave velocity (measures of arterial stiffness) despite unfavorable increases in visceral fat. A plausible explanation for this finding may be that although

visceral fat increased in the HIIT group, this was not accompanied by an increase in intrahepatic triglyceride content which has been shown to be a better marker of metabolic derangements associated with obesity and diabetes (Fabbrini et al., 2009). This theory is further supported by a trend towards a reduction in triglycerides in the HIIT group. High-intensity exercise has been shown to increase lipoprotein lipase activity and facilitate triglyceride clearance resulting in lower circulating triglycerides in the blood (Freese et al., 2011). It is also plausible that improvements in arterial stiffness associated with HIIT occur completely independent of changes in body composition. The favorable improvements in arterial stiffness with just 4 weeks of training with HIIT but not MICT is a novel finding in that experts had previously suggested that moderate-intensity aerobic exercise (55% of VO_{2max}) may be more suitable than high-intensity exercise (80-85% of VO_{2max}) for improving arterial stiffness in obese populations (Montero, Roberts, & Vinet, 2014) due to lower sympathetic activity.

The results for glucose and insulin do not support my hypothesis that MICT and HIIT would yield superior effects on glycemic control compared to control during the intervention. In contrast, 2-h iAUC for glucose was significantly reduced and 2-h iAUC for insulin was unchanged following 4-weeks of fat-sugar supplement in control group. These findings were not anticipated since previous studies have demonstrated a large significant increase in iAUC for insulin during OGTT in the control condition following 7-14 days of overfeeding (Knudsen et al., 2012; Walhin et al., 2013). There are several plausible explanations for observing no change in the control group during the current study. First, the control group significantly reduced habitual energy and sugar intake during the intervention. Second, our control group did not reduce physical activity by

6,000-8,500 steps/day as was done in the aforementioned studies (Knudsen et al., 2012; Krogh-Madsen et al., 2014; Walhin et al., 2013). Lastly, the overweight/obese subjects in the current study may have been resistant to the adverse metabolic effects that typically accompany modest weight gain because they were metabolically normal at baseline (Fabbrini et al., 2015). A recent study by Fabbrini et al. (2015) demonstrated that metabolically normal (normal intrahepatic triglyceride content and insulin sensitivity) obese individuals did not suffer any metabolic deterioration after a modest weight gain (+6% of initial body weight) induced by a high-caloric diet. In contrast, metabolically abnormal (high intrahepatic triglyceride content and insulin resistance) obese individuals exhibited increased blood pressure and plasma triglyceride levels, and decreased insulin sensitivity in liver, skeletal muscle, and adipose tissue. The results of the current study suggest that a daily fat-sugar supplement of +606 kcal/day without a concomitant reduction in physical activity is not enough to induce a deleterious change in insulin action and glycemic control in healthy overweight/obese males.

Although glucose and insulin responses were not significantly different, hepatic IRI and 30-min insulin were significantly increased in control and decreased in MICT after the intervention. This suggests that MICT may have improved hepatic insulin sensitivity despite the fat-sugar supplement. Diets rich in fat and sugar have typically been shown to induce insulin resistance via increases in de novo lipogenesis and increased accumulation of intrahepatic triglycerides, with subsequent reductions in peripheral glucose uptake (Rabol, Petersen, Dufour, Flannery, & Shulman, 2011). The prevention of hepatic insulin resistance via MICT is not unexpected in that it has previously been demonstrated that a single bout of exercise increases hepatic insulin

sensitivity causing a reduction in endogenous glucose production to improve glycemic control (Devlin, Hirshman, Horton, & Horton, 1987). Krogh-Madsen et al. (2014) previously demonstrated that worsened glycemic control in the control group was due in part to increases in endogenous glucose production after 14 days of overfeeding, suggesting that excess intake induced hepatic insulin resistance. Furthermore, 12 weeks of exercise training has been shown to prevent free fatty acid-induced insulin resistance in obese individuals (Haus et al., 2010). Further studies using hyperinsulinemic clamp or OGTT with tracers are needed to verify these findings.

The results for cardiorespiratory fitness (VO_{2peak}) support my hypothesis that both MICT and HIIT would yield superior improvements in cardiorespiratory fitness compared to sedentary control during 4 weeks of fat-sugar supplemented feeding. However, the increases in VO_{2peak} with HIIT (+0.39 L/min, ~12% improvement) were not significantly greater than the increases in VO_{2peak} with MICT (+0.3 L/min, ~10% improvement) which does not support my hypothesis that HIIT would be superior compared to MICT. Although most previous studies (Kessler et al., 2012; Weston et al., 2014) indicate that HIIT is superior to MICT for improving VO_{2peak}, there are several exceptions in the literature (Ciolac et al., 2010; Currie, Dubberley, McKelvie, & MacDonald, 2013; Poole & Gaesser, 1985). In particular, Poole and Gaesser (1985) showed equivalent improvements in VO_{2max} after 4 weeks of MICT (55 minutes on 3 days/week at 50% of VO_{2max}) and HIIT (10 X 2-min intervals at 105% of VO_{2max} with 2 min rest between intervals) on a cycle ergometer in young recreationally active young males, with both groups improving VO_{2max} by ~17% despite a major difference in exercise intensity. However, it is important to note that previous studies that have

compared HIIT and MICT for improving VO_{2peak} occurred while subjects were following a habitual diet and not during a high fat, high sugar intake as was done in the current study.

The only two previous studies that assessed changes in cardiorespiratory fitness (VO_{2peak}) during a short period of high fat (Ortega et al., 2013) or high fat-sugar intake (Black, 2013) demonstrated similar findings to the current study. Ortega et al. (2013) showed that eleven 55-min sessions of high-intensity continuous cycling (65% VO_{2max}) during 2 weeks of high saturated fat intake increased VO_{2peak} (+0.46 L/min, +16%) in overweight adults. These increases in VO_{2peak} (+16%) were higher than observed with HIIT (+12%) in the current study, most likely due to a lower baseline VO_{2peak} and higher training session frequency in the Ortega et al. (2013) study. Similarly, Black (2013) demonstrated that 12 sessions of exercise training (6 sessions of MICT at 75% of HR_{peak} and 6 sessions of HIIT at 90-95% of HR_{peak}) during 3 weeks of high fat-sugar intake increased VO_{2peak} (+0.24 L/min, +8%). The improvements in VO_{2peak} were slightly lower than those observed in the current study most likely due to the shorter study duration (3 weeks). Taken together with the results of my study, these findings suggest that dietary quality does not adversely affect improvements in cardiorespiratory fitness that typically accompany exercise training.

Improvements in VO_{2peak} with exercise training may have greater clinical significance than minor changes in cardiometabolic risk factors typically associated with poor diet quality (Heroux et al., 2010; Kouki et al., 2012). A recent meta-analysis totaling over 77,000 men and 15,000 women revealed that individuals who were fit had a two-fold lower risk of mortality compared to those who were unfit, regardless of BMI (Barry

et al., 2014). Furthermore, a 1-MET (3.5 ml/kg/min VO_2) improvement in cardiorespiratory fitness is associated with a 15% reduction in all-cause mortality and a 13% reduction in cardiovascular events (Kodama et al., 2009). The current study demonstrates that 4 weeks of exercise training yields a 0.94 (+3.3 ml/kg/min) and 1.06 MET (+3.7 ml/kg/min) improvement in cardiorespiratory fitness with MICT and HIIT respectively, despite a diet high in fat and sugar. These findings are consistent with previous findings that suggest that the health benefits of exercise training and/or cardiorespiratory fitness are independent of diet quality (Heroux et al., 2010; Kouki et al., 2012). Although exercise training did not yield superior improvements in body composition and most of the cardiometabolic risk factors examined in this study, the improvements in cardiorespiratory fitness exhibited by exercise training may be of greater clinical importance when examined in the context of all-cause or cardiovascular disease mortality.

Strengths and Limitations

A strength of this study is that the intervention protocol (+606 kcal/day and 4 days/week of exercise training) has more ecological value than previous studies that have examined the simultaneous effects of exercise and high caloric intake (Krogh-Madsen et al., 2014; Walhin et al., 2013). Increasing daily energy intake by 1,500 to 2,000 kcal/day and reducing daily step counts in a control group by 70-85% (Knudsen et al., 2012; Krogh-Madsen et al., 2014; Walhin et al., 2013) may provide valuable mechanistic insight for understanding the pathogenesis of obesity, cardiovascular disease and diabetes. However, the likelihood of any individual increasing energy intake and reducing physical activity by this amount over the course of a few weeks is extremely

unlikely. I believe that an additional 606 kcal/day, primarily in the form of fat and sugar, better simulates a period of overeating such as the holidays. Furthermore, the MICT and HIIT protocols closely approximate the ACSM recommendations of 150 min per week of moderate-intensity and 75 min of high-intensity exercise per week, respectively (Garber et al., 2011). Another strength of this study is the inclusion of a more at-risk population (inactive, overweight/obese). Previous studies (Krogh-Madsen et al., 2014; Walhin et al., 2013) assessing overfeeding and exercise training have included young, fit males (VO_{2max} >55 ml/kg/min) who are not as susceptible to weight gain during periods of excess intake as compared to those who are overweight/obese (Hull, Radley et al., 2006; Stevenson et al., 2013; Yanovski et al., 2000). Other strengths of this study include: the use of DXA (considered to be the practical gold standard) to track changes in body composition, supervision of all exercise training sessions (100% completion rate), objective tracking of habitual physical activity with accelerometers, and fat-sugar supplements (donuts) were given directly to the subjects.

A limitation of this study is that all meals were not provided to subjects. The data from food records in this study (Figure 8) indicate that the control group compensated by decreasing habitual dietary intake. Feeding all meals to subjects would have been extremely costly but it most likely would have improved precision and prevented the dietary compensation observed in the control group. In addition, food records have been shown to be very inaccurate for tracking energy intake (Lichtman et al., 1992; Schoeller et al., 1990) with some experts recently suggesting that self-report measures of energy intake are unsuitable and should not be used at all (Dhurandhar et al., 2015; Freedman et al., 2014). Another limitation of this study is that the majority of our subjects were

metabolically normal overweight/obese at baseline. It was recently demonstrated that metabolically normal overweight/obese individuals may be resistant to the adverse metabolic effects of modest weight gain (Fabbrini et al., 2015). Finally, habitual energy intake and expenditure were not tracked continuously for the entire study. Therefore, it is possible that compensation in habitual diet or exercise went unnoticed during weeks 1-3 of the intervention. This study included healthy, inactive overweight and obese males. Thus applicability of these findings to other populations, such as females, older adults or patients with chronic disease is unknown.

CHAPTER 6

CONCLUSION

The results of this study show that the addition of a fat-sugar supplement of ~14,500 kcal over a four-week period was not sufficient to induce deleterious changes in body composition and cardiometabolic health in overweight/obese young males. A potential explanation for the lack of significant findings may in part be due to a compensatory down-regulation of habitual energy intake in the control group which was not observed in the exercise conditions during the intervention. Furthermore, exercise training did not afford overweight/obese males additional health benefits, with the exception of improvements in cardiorespiratory fitness and preservation of hepatic insulin sensitivity. Whether these findings extend to other populations such as women and those at risk of cardiovascular disease or diabetes remains to seen. Future studies examining the ability of exercise training to prevent deleterious health effects associated with fat-sugar supplements should provide all meals to subjects and consider tracking total energy expenditure with doubly labeled water.

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APPENDIX A

CONSENT FORM AND IRB APPROVAL

CONSENT FORM

Effects of a fat-sugar supplemented diet, with and without exercise training, on body composition, glycemic control, vascular function and other blood markers of cardiovascular risk in overweight and obese, sedentary males.

INTRODUCTION
The purposes of this form are to provide you (as a prospective research study participant) information that may affect your decision as to whether or not to participate in this research and to record the consent of those who agree to be involved in the study.

RESEARCHERS
Glenn Gaesser, PhD, a professor, and Wesley Tucker, and Catherine Lee Jarrett, doctoral students, in the Physical Activity, Nutrition and Wellness Program in the School of Nutrition and Health Promotion, have requested your participation in a research study.

STUDY PURPOSE
Our primary objective is to determine whether exercise training can prevent the anticipated deleterious effects of a donut supplemented diet in healthy overweight and obese men.

DESCRIPTION OF RESEARCH STUDY
If you decide to participate, then as a study participant you will join a study involving research on the effects of either moderate or vigorous exercise training on body weight, body fat, blood lipids, blood glucose, and cardiovascular disease risk factors while supplementing your diet with daily donuts.

You are being asked to participate in this study because you are considered as overweight or obese by current public health guidelines, (BMI >25 kg/m^2), male, and 18 - 50 years of age, in good health, and capable of performing vigorous physical activity. You must also be willing to consume 2 donuts per day, 6 days per week, for 4 weeks. If your age is within the range of 46-50, you may be required to obtain written approval from your doctor in order to participate.

As a study participant you will have between 15 and 19 total visits to the Health Lifestyles Laboratory on the Downtown Phoenix campus of ASU. The number of visits depends on whether you are (randomly) assigned to the Control Group (15 visits) or either of the two Exercise Training Groups (19 visits).

Visit 1 (Consent & Screening):
Your first visit will involve coming to the test site where the study will be explained to you, we will answer any questions you may have and you will be asked to sign this consent. When the consent is signed you will go through the following screening tests to confirm that you are eligible for the study:
1. Fill out and sign a questionnaire called the PAR-Q to acknowledge that you are suitable to perform exercise. If you answer "Yes" to any of the questions on the PAR-Q you will need to obtain permission from a physician to participate in this study.
2. Measurement of your height, weight, blood pressure and blood glucose to ensure that you meet the criteria of participation.
3. We will conduct the flow-mediated dilation (FMD) procedure (see below) to make sure we can see the artery in your arm.
4. You will be asked to wear a small movement sensor for one week to measure your physical activity.
5. You will be asked to fill out a Three-day Food Record during the next week.
6. You will be given a stool collection kit, including instructions, in order to provide the study investigators with a stool sample when you arrive for visit 2. A second stool sample will be requested at the end of the study.
This visit will take approximately 75 minutes.

Testing:

Initial here

All testing will be completed at baseline and after 4-weeks for both the exercise training and control groups.

Measurement of Physical Activity and Dietary Intake
We will be measuring your movement and dietary intake at different times throughout the study by using a small movement senor called an accelerometer and having you fill out a three-day food record. We will have you wear the accelerometer for a week before you start as well as during the 2nd and 4th weeks of the study for a total of 3 weeks of wear time. This device is worn on your waist during the day. The device is very light, easy to wear, and easy to conceal. Also, to assess your dietary intake we will have you fill out a three-day food record for a week before you start as well during the 2nd and 4th weeks of the study for a total of 3 weeks of diet logs. You will record everything you eat and drink for 2 weekdays and 1 weekend day during the weeks that you are required to keep a three-day food record.

Analysis of Stool Samples
Intestinal microbes will be assessed by measuring the presence of different microbial groups in fecal samples collected during the study. The types and quantities of microbes present in your intestine can influence your health and may change with exercise and dietary modifications. You will be asked to collect a total of 2 samples during the study (once at the beginning and once at the end). A stool collection kit that contains everything you need to collect the samples will be provided to you by the study staff. You will have the option of collecting your sample at home (you will be required to deliver your sample to the Arizona Biomedical Collaborative) or at the Arizona Biomedical Collaborative building at 425 North 5th Street, Phoenix, AZ 85048 during visit 2 and visit 14 (if you are in the Control Group) or visit 2 and visit 18 (if you are in one of the Exercise Training Groups). Samples collected at home must be kept cold so you will be provided with a cooler and ice packs which must be returned with the sample within 24 hours of collection.

Baseline and 4-Week Testing (Visits 2 and 15 (Control Group); Visits 2 and 19 (Exercise Training Groups):

- You will need to arrive at the laboratory in a **fasted state** (nothing but water after 10 PM)
- You will be asked to not drink any **caffeine, alcohol or dietary supplements** for 48 hours prior to arrival at the laboratory for this visit.

- Resting blood pressure will be measured using an automated blood pressure machine.

- Central and Arm Blood Pressures & Pulse Wave Measurement:
  This procedure involves placing a blood pressure cuff on your upper arm and connecting the cuff to a device called the SphygmaCor. This measures the blood pressure in your arm and the central body (heart, kidneys etc.). All measurements are made while lying quietly on a table in a dimly lit room for 20 minutes. To measure your pulse wave we will place a blood pressure cuff on the upper thigh of your left leg. You may feel a small amount of pressure as we feel for your pulse at the top of your leg (femoral) and your neck (carotid) to locate both arteries. After locating each artery we will make measurements between the blood pressure cuff, and the respective arteries. Finally, we will gently place a small probe on the skin over the artery in your neck which will cause the blood pressure cuff on the leg to inflate. Carotid and femoral artery waveforms are detected to calculate carotid-femoral pulse wave velocity, a measurement of arterial stiffness. This test takes about 45 minutes.

- Brachial Artery Flow-Mediated Dilation:
  This procedure involves taking ultrasound images of an artery in your upper arm before, during, and after a blood pressure cuff is inflated around your forearm. After lying quietly on a padded ultrasound table for 20 minutes, a blood pressure cuff will be positioned on your forearm. After recording baseline

Initial here

ultrasound measures on your upper arm, the blood pressure cuff will be inflated and kept in place for 5 minutes. You may experience a tingling feeling in your hand, which is normal. The blood pressure cuff will then be deflated rapidly and ultrasound measures will be taken for 5 minutes.
This test takes about 30 minutes.

- Muscle size:
  We will measure the size of your muscles in your upper leg and the angle of muscle fibers within these muscles, using ultrasound imaging. You will be asked to lie down on a padded examination table and relax for 20 minutes. During this time the researcher will measure and mark imaging sites along the upper leg, using a tape measure and medical marker. Next, the researcher will place the ultrasound device on the skin and proceed to capture pictures of the upper leg muscles. We will take these measures on one of your legs. This test should last 15-20 minutes.

- Dual-Energy X-ray Absorptiometry (DEXA)
  Your body composition (amounts of fat and lean tissue) will be determined by using a bone density measurement machine, called a Dual-energy X-ray Absorptiometry (DEXA). You will be asked to lie face up, on a padded table for about 7 minutes while the scanner arm of the DEXA machine passes over your entire body. The scanner will not enclose you or touch you, and you can wear regular clothing (no metal allowed). A certified X-ray technician will complete all DEXA scans.
  This test takes about 15 minutes.

- Oral Glucose Tolerance Test (OGTT)
  You will be asked to report for each OGTT (visits 2 and 15 for Control group; visits 2 and 19 for Exercise Training group) in the morning following an overnight fast (i.e., nothing but water after 10 PM). An OGTT allows us to assess blood sugar control and insulin sensitivity before and after you complete the intervention. A small plastic catheter will be placed into a vein in your forearm. You will drink a sugary orange drink. Blood samples will be collected from the catheter before the drink and every 30 minutes after the drink for 2 hours. We will draw approximately 40ml (8tsp) of blood to measure blood markers before and after the intervention. All OGTTs and blood draws will be performed by a highly trained nurse and certified phlebotomist. This test takes about 3 hours.

  You will be fed a small lunch consisting of a Clif Bar, Chips and a Drink at this point.

- Maximal Exercise Test: For this test, you will be wearing a mask attached to a hose that collects the air you breathe out. You will also wear a heart rate monitor that consists of an elastic strap that wraps around your chest to measure your heart rate. You will sit quietly on the stationary bicycle for 2 minutes then you will be asked to pedal at light resistance for 5 minutes for the warm-up phase. After the warm-up phase the resistance will increase continuously every minute until you cannot continue. We will encourage you to push yourself as hard as you feel comfortable. After a 10 minute rest period you will perform an "all-out" bout of exercise at the same resistance you ended at on the previous test. Again you will push yourself as hard as you feel comfortable with until you are exhausted.
  The whole test will take about 30 minutes.

- Muscle testing:
  We will determine the muscle function on one of your legs. This exercise will be performed for one leg on a specialized piece of exercise equipment. For this test, you will be seated on the exercise equipment and strapped in around your shoulders and hips to keep you in position. One of your legs will be attached to the leg attachment with a padded ankle strap. For this test, you will be asked to move your knee from a bent position to a straighten position and then from a straightened position to a bent position using your leg muscles to push and pull the bar as hard as you can in both directions. For a separate test, you will be asked to push against a stationary bar as hard as you can.
  This test should last 15-20 minutes.

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Total time for visit 2 is approximately 6 hours

Exercise Training (Visits 3 through 18 for Exercise Training Groups)
If you are randomized into either of the exercise groups you will be asked to complete 4 exercise sessions per week for 4 weeks for a total of 16 exercise sessions. These training sessions will include either: 4 high-intensity interval exercise training session OR 4 continuous steady-state exercise training sessions per week. All exercise will be conducted on an exercise bicycle. Training days and times will be flexible, according to your schedule.

- Moderate-intensity Continuous Exercise Training (4 times per week):
  - Approximately 150 min/week of moderate-intensity continuous exercise on an exercise bicycle. Participants will report to the Exercise Lab on 4 days/week and do ~38 min of moderate-intensity exercise on the exercise bicycle.

- High-intensity Interval Exercise Training (4 times per week):
  - Approximately 80 min/week of high-intensity interval exercise consisting of ten, 1-minute high-intensity sprints, separated by 1 minute of light active recovery. Participants will report to the Exercise Lab on 4 days/week and do ~20 min of high-intensity interval exercise on the exercise bicycle.

Each exercise session will begin with a 5 min light-intensity warm-up and finish with a 5-minute light-intensity cool-down.

Total time for each exercise training visit is approximately 45 min (Moderate-intensity continuous exercise group) and 30 min (High-intensity Interval exercise group).

Control Group

- If you are randomly assigned to the control group you will be asked to maintain your current physical activity level for the 4-week period during which you will be consuming the donuts. After the final post-intervention testing, you will have the opportunity to participate in one of the two exercise programs described above. Participation is voluntary. If you decide to participate, you will have your choice of either of the exercise training programs described above. The only additional assessment would be body weight and body fat at the completion of these 4 weeks of optional exercise training.

Physical Activity Enjoyment Scale (PAES):

If you are randomized to one of the two exercise training groups, you will be given the Physical Activity Enjoyment Scale to complete after your final exercise training session to assess whether there are differences in perceived enjoyment between the different forms of exercise trainings.

Donut Pickup (Visits 3 through 14 for Control Group; Visits 3, 4, 6, 7, 8, 10, 11, 12, 14, 15, 16, and 18 for Exercise Training Groups)

You will be asked to consume 2 donuts per day, 6 days per week, for 4 weeks. Donuts will be purchased by the study researchers at a local Dunkin Donuts on Monday, Wednesday and Friday morning of each week. You will be required to come to the Exercise laboratory on Monday, Wednesday, and Friday of each week for donut pickup. This visit can be part of your regular exercise training visit if you are in either of the two Exercise Training groups. On each occasion you will be given 4 donuts to consume over the next two days. You will be provided a menu of donut options so that you will be able to choose the types of donuts that you would like

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most to consume. You may consume the donuts at any time of the day that you choose. We ask that you not consume all 4 donuts in one day.

Total time commitment for completion of the study is approximately 12 hours if you are in the Control Group and approximately 22 hours if you are in the Exercise Training Groups.

RISKS

Research studies often involve some risks. The risks of exercise include local muscle soreness, abnormal changes in blood pressure, nausea, faintness, dizziness, irregular heartbeats (rare), and, in very rare instances, heart attack.

You will be monitored by trained investigators and if there are any adverse effects, the exercise testing or the exercise session will be halted. All exercise testing procedures will comply with the guidelines for exercise test administration as recommended by the American College of Sports Medicine and required by the Healthy Lifestyles Research Center at Arizona State University. You will be asked not to attempt any exercise that you feel is beyond your physical abilities. If you experience discomfort, feel you are unable to continue or wish to stop an exercise at any point, you are requested to inform the investigator immediately.

During the DXA scan you will be exposed to minimal radiation (1-4 microSieverts) that is within an acceptable range as provided by the FDA. Anytime you are exposed to radiation there is a potential risk. The amount of radiation (1-4 microSieverts) that you would be exposed to is very minimal. For example, you would receive radiation exposure of approximately 80 microSieverts on a transatlantic airline flight of 8 hours, 50 microSieverts living in Denver, Colorado, at an elevation of 5,000 feet for approximately 4 weeks, or 30 to 40 microSieverts during a typical chest x-ray.

The OGTT involves a needle puncture in your forearm and hence may lead to some discomfort and bruising as well as a slight risk of infection. These procedures will be carried out by experienced medical staff who will properly clean the insertion site and use standard sterile technique during the procedures. Other possible risks of a blood draw include dizziness, fainting, nausea, and vomiting. All blood draws will be conducted while you are seated to ensure your safety in case any of these possible side effects occur.

There is a possible chance of weight gain as a result of potentially higher daily caloric intake. Additionally, a fat-sugar supplemented diet may lead to impairment of glycemic control, vascular function and blood pressure.

You may come into contact with your stools during collection. This risk will be minimized by providing you with gloves and other collection tools which prevent contact with your samples. You will be encouraged to wash your hands thoroughly following sample collection.

As with any research, there is some possibility that you may be subject to risks that have not yet been identified.

BENEFITS

Although there may be no direct benefits to you, you will be provided information on your test results and the study results if you would like us to contact you when the study is complete.

NEW INFORMATION

If the researchers find new information during the study that would reasonably change your decision about participating, then they will provide this information to you.

CONFIDENTIALITY

All information obtained in this study is strictly confidential unless disclosure is required by law.

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The results of this research study may be used in reports, presentations, and publications, but your name or identity will not be revealed. In order to maintain confidentiality of your records, Dr. Gaesser will use subject codes on all data collected, maintain a master list separate and secure from all data collected, and limit access to all confidential information to the study investigators.

WITHDRAWAL PRIVILEGE

It is ok for you to say no. Even if you say yes now, you are free to say no later, and withdraw from the study at any time. Your decision will not affect your relationship with Arizona State University or otherwise cause a loss of benefits to which you might otherwise be entitled.
Your participation is voluntary and if you decide not to participate or decide to withdraw from the study it will not affect your grade, treatment, care, employment status.

COSTS AND PAYMENTS

All study procedures will be provided to you at no cost. If you are randomized to the control group you will be paid $50 (cash or gift card) for completion of the study, including all testing visits and successful pickup of doughnuts on three days each week. If you are in either of the two exercise training groups you will be paid $100 (cash or gift card) for completion of the study, including both testing visits and all exercise training sessions. Participants will also receive 4 dozen donuts to consume during the 4 weeks of the study. Partial payment will be made in the following manner if you only complete some of the visits:

- Control group: completion of baseline testing but failure to complete the final testing visit: $25
- Exercise training groups: completion of baseline testing and some or all of the exercise training sessions, but failure to complete the final testing visit: $50

COMPENSATION FOR ILLNESS AND INJURY

If you agree to participate in the study, then your consent does not waive any of your legal rights. However, no funds have been set aside to compensate you in the event of injury. In the event of a medical emergency first aid will be administered and if necessary, 911 will be called.

VOLUNTARY CONSENT

Any questions you have concerning the research study or your participation in the study, before or after your consent, will be answered by Dr. Glenn Gaesser, 500 N 3rd ST, Phoenix, AZ 85004; 602-827-2283; glenn.gaesser@asu.edu.

If you have questions about your rights as a subject/participant in this research, or if you feel you have been placed at risk, you can contact the Chair of the Human Subjects Institutional Review Board, through the ASU Office of Research Integrity and Assurance, at 480-965 6788.

This form explains the nature, demands, benefits and any risk of the project. By signing this form you agree knowingly to assume any risks involved. Remember, your participation is voluntary. You may choose not to participate or to withdraw your consent and discontinue participation at any time without penalty or loss of benefit. In signing this consent form, you are not waiving any legal claims, rights, or remedies. A copy of this consent form will be given to you.

Your signature below indicates that you consent to participate in the above study

_____ _____ _____

_____
Initial here

Subject's Signature Printed Name Date

_____ _____

Contact phone number E-mail

INVESTIGATOR'S STATEMENT

"I certify that I have explained to the above individual the nature and purpose, the potential benefits and possible risks associated with participation in this research study, have answered any questions that have been raised, and have witnessed the above signature. These elements of Informed Consent conform to the Assurance given by Arizona State University to the Office for Human Research Protections to protect the rights of human subjects. I have provided the subject/participant a copy of this signed consent document."

Signature of Investigator_____ Date_____

_____

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APPENDIX B

PHYSICAL ACTIVITY READINESS QUESTIONNAIRE

Physical Activity Readiness Questionnaire - PAR-Q (revised 2002)

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES	NO	
☐	☐	1. **Has your doctor ever said that you have a heart condition <u>and</u> that you should only do physical activity recommended by a doctor?**
☐	☐	2. **Do you feel pain in your chest when you do physical activity?**
☐	☐	3. **In the past month, have you had chest pain when you were not doing physical activity?**
☐	☐	4. **Do you lose your balance because of dizziness or do you ever lose consciousness?**
☐	☐	5. **Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?**
☐	☐	6. **Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?**
☐	☐	7. **Do you know of <u>any other reason</u> why you should not do physical activity?**

If you answered YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to <u>all</u> PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active – begin slowly and build up gradually. This is the safest and easiest way to go.
- take part in a fitness appraisal – this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

→ **DELAY BECOMING MUCH MORE ACTIVE:**

- if you are not feeling well because of a temporary illness such as a cold or a fever – wait until you feel better; or
- if you are or may be pregnant – talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

<u>Informed Use of the PAR-Q</u>: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

NAME _____

SIGNATURE _____ DATE _____

SIGNATURE OF PARENT or GUARDIAN (for participants under the age of majority) _____ WITNESS _____

Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.

CSEP | SCPE

APPENDIX C

RECRUITMENT FLYER

ARIZONA STATE UNIVERSITY

Healthy Sedentary Men 18 – 50 years old and over a certain body weight are needed for a study investigating the effects of different exercise protocols on body weight and cardiovascular health during 4 weeks of modestly increased calorie intake

Compensation: $50-$100 + 48 Free Donuts

This study is designed to determine the effects of different aerobic exercise protocols on body weight and several measures of cardiovascular health during 4 weeks while supplementing regular diet with 2 donuts per day, 6 days per week . This study includes 15-19 visits to the Healthy Lifestyles Research Center on the Arizona State University Downtown Campus in Phoenix. Time commitment: 11-22 hours over the course of 5 weeks. **Your participation throughout the study is completely voluntary.**

Eligible men must be nonsmokers, in good health, have no restrictions for participating in vigorous intensity physical activity, and must not be taking any medications for blood pressure, cholesterol, diabetes or a heart condition. **If your weight is greater than the number indicated for your height, you may qualify for this study:**

Height	5'3"	5'4"	5'5"	5'6"	5'7"	5'8"	5'9"	5'10"	5'11"	6'0"	6'1"	6'2"	6'3"	6'4"	6'5"
Weight (pounds)	141	146	150	155	160	165	169	174	179	184	190	195	200	205	210

Please contact:

Wesley Tucker (602 827-2492; wjtucker@asu.edu) or
Catherine Jarrett (602 827-2492; Catherine.Jarrett@asu.edu)

Wesley Tucker 602-827-2492 wjtucker@asu.edu	Wesley Tucker 602-827-2492 wjtucker@asu.edu	Wesley Tucker 602-827-2492 wjtucker@asu.edu	Wesley Tucker 602-827-2492 wjtucker@asu.edu	Wesley Tucker 602-827-2492 wjtucker@asu.edu	Wesley Tucker 602-827-2492 wjtucker@asu.edu	Wesley Tucker 602-827-2492 wjtucker@asu.edu	Wesley Tucker 602-827-2492 wjtucker@asu.edu	Wesley Tucker 602-827-2492 wjtucker@asu.edu	Wesley Tucker 602-827-2492 wjtucker@asu.edu	Wesley Tucker 602-827-2492 wjtucker@asu.edu	Wesley Tucker 602-827-2492 wjtucker@asu.edu	Wesley Tucker 602-827-2492 wjtucker@asu.edu

APPENDIX D

SCREENING QUESTIONNAIRE

Dunkin Donuts and Exercise Study

Screening Questions

1. Age: Males must be between 18 and 45. Age: _____
2. BMI: >25. Height: _____ Weight: _____ BMI: _____
3. Blood Pressure: <160/100 mmHg Blood Pressure:_____
4. Fasting Blood Glucose: <126 mg/dl Blood Glucose: _____
5. FMD Acoustic Window: _____
6. Medications: Heart, blood pressure, diabetes, thyroid.
7. History: personal history of heart attack, angina, stroke, fainting during exercise, hypercholesterolemia, hypertriglyceridemia.
8. Current exercise routine: must be relatively sedentary; Willing to keep same routine outside of study.
9. Diet: Must be willing to keep current diet and make no changes throughout the course of the study
10. Schedule: must be able to do 2 fasting visits early in morning during the week. Last visit 48 hours after last training session.
11. Timeline: need to have 4-5 weeks available not going out of town for more than a few days

APPENDIX E

THREE-DAY FOOD RECORD

Three-Day Food Record

A food record is designed to get an accurate description of your diet. Please try to be as accurate as possible by recording all of the foods and beverages you eat and drink, including condiments such as ketchup, mustard, coffee creamer, etc. Record the exact amount of food eaten and important variations (ex. skim, 2%, reduced fat, sugar-free, etc). If the food is prepared at home or in a restaurant, please include a description of the preparation techniques (ex. grilled vs. fried) and the name of the item on the restaurant's menu.

Day 1 Food Record (Date: _____)

Time	*Food & Beverage Description*	*Amount eaten*

1

Day 2 Food Record (Date: _____)

Time	*Food & Beverage Description*	*Amount eaten*

Day 3 Food Record (Date: _____)

Time	*Food & Beverage Description*	*Amount eaten*

5

APPENDIX F

MODERATE-INTENSITY CONTINUOUS TRAINING LOG

Donut and Exercise Study
Subject ID: DD_____

Target Heart Rate Range:

Wk 1	Session 1								Session 2							
HR																
KP																
RPM																
Wk 1	Session 3								Session 4							
HR																
KP																
RPM																
Wk 2	Session 1								Session 2							
HR																
KP																
RPM																
Wk 2	Session 3								Session 4							
HR																
Kp																
RPM																
Wk 3	Session 1								Session 2							
HR																
KP																
RPM																
Wk 3	Session 3								Session 4							
HR																
KP																
RPM																
Wk 4	Session 1								Session 2							
HR																
KP																
RPM																
Wk 4	Session 3								Session 4							
HR																
Kp																
RPM																

Seat Height:

APPENDIX G

HIGH-INTENSITY INTERVAL TRAINING LOG

Donut and Exercise Study

Subject ID: DD

Date	
Week	
Session of Week	

Time	Description	Heart Rate	Resistance	RPM
1	Warm up			
2	Warm up			
3	Warm up			
4	Warm up			
5	Warm up			
6	Interval 1			
7	Rest 1			
8	Interval 2			
9	Rest 2			
10	Interval 3			
11	Rest 3			
12	Interval 4			
13	Rest 4			
14	Interval 5			
15	Rest 5			
16	Interval 6			
17	Rest 6			
18	Interval 7			
19	Rest 7			
20	Interval 8			
21	Rest 8			
22	Interval 9			
23	Rest 9			
24	Interval 10			
25	Rest 10			
26	Cool Down			
27	Cool Down			
28	Cool Down			
29	Cool Down			
30	Cool Down			

Date	
Week	
Session of Week	

Time	Description	Heart Rate	Resistance	RPM
1	Warm up			
2	Warm up			
3	Warm up			
4	Warm up			
5	Warm up			
6	Interval 1			
7	Rest 1			
8	Interval 2			
9	Rest 2			
10	Interval 3			
11	Rest 3			
12	Interval 4			
13	Rest 4			
14	Interval 5			
15	Rest 5			
16	Interval 6			
17	Rest 6			
18	Interval 7			
19	Rest 7			
20	Interval 8			
21	Rest 8			
22	Interval 9			
23	Rest 9			
24	Interval 10			
25	Rest 10			
26	Cool Down			
27	Cool Down			
28	Cool Down			
29	Cool Down			
30	Cool Down			

Date	
Week	
Session of Week	

Time	Description	Heart Rate	Resistance	RPM
1	Warm up			
2	Warm up			
3	Warm up			
4	Warm up			
5	Warm up			
6	Interval 1			
7	Rest 1			
8	Interval 2			
9	Rest 2			
10	Interval 3			
11	Rest 3			
12	Interval 4			
13	Rest 4			
14	Interval 5			
15	Rest 5			
16	Interval 6			
17	Rest 6			
18	Interval 7			
19	Rest 7			
20	Interval 8			
21	Rest 8			
22	Interval 9			
23	Rest 9			
24	Interval 10			
25	Rest 10			
26	Cool Down			
27	Cool Down			
28	Cool Down			
29	Cool Down			
30	Cool Down			

Date	
Week	
Session of Week	

Time	Description	Heart Rate	Resistance	RPM
1	Warm up			
2	Warm up			
3	Warm up			
4	Warm up			
5	Warm up			
6	Interval 1			
7	Rest 1			
8	Interval 2			
9	Rest 2			
10	Interval 3			
11	Rest 3			
12	Interval 4			
13	Rest 4			
14	Interval 5			
15	Rest 5			
16	Interval 6			
17	Rest 6			
18	Interval 7			
19	Rest 7			
20	Interval 8			
21	Rest 8			
22	Interval 9			
23	Rest 9			
24	Interval 10			
25	Rest 10			
26	Cool Down			
27	Cool Down			
28	Cool Down			
29	Cool Down			
30	Cool Down			

APPENDIX H

PULSE WAVE VELOCITY ACQUISITION NOTES

PWV/AIX Acquisition Notes

DD # _____ DOB: _____

Height: _____ cm Weight: _____ kg BMI: _____ kg/m² Age: _____ y

---

Technician: _____ Date: ___/___/_____ Time: _____ am/pm

Fasted? Y / N

Days since last exercise bout: _____

Cuff size used: _____

Resting

0min	RHR:	BP: /
10min	RHR:	BP: /
15min (or 1st Measure)	RHR:	BP: /

Measures

1st	2nd	3rd
RHR:	RHR:	RHR:
BP: /	BP: /	BP: /
AP:	AP:	AP:
AIX@75:	AIX@75:	AIX@75:
CBP: /	CBP: /	CBP: /
AIX:	AIX:	AIX:
PWV:	PWV:	PWV:

APPENDIX I

BRACHIAL ARTERY FLOW-MEDIATED DILATION SETTINGS NOTES

Brachial Artery Ultrasound Subject Settings

Study _____ Subject ID _____ Date _____ Time _____

Arm Used	
Cuff Size	
Distance from medial epicondyle of humerus (measure from distal side of probe)	
Frequency	
Depth (cm)	
Focal Zone setting (how many and location i.e: @)	
Compression	
Noise Rejection	
Gain (# of ticks right or left of midline)	
Zoomed? how much of the visible artery pre-zoom)	
SV Size	
Steering Angle	-15
Correction Angle	60
Baseline	
Angle of Probe (acute/obtuse with table closest to sonographer)	

Time Gain Compensation (sliders)
Insert a line where each is moved
If not moved no line is needed

_____
_____
_____
_____
_____
_____
_____
_____

Additional notes on subject and settings:

APPENDIX J

PHYSICAL ACTIVITY ENJOYMENT SCALE

A reproduction of the Physical Activity Enjoyment Scale questionnaire demonstrating the 7-point bipolar scale.

* I enjoy it	1	2	3	4	5	6	7	I hate it
I feel bored	1	2	3	4	5	6	7	I feel interested
I dislike it	1	2	3	4	5	6	7	I like it
* I find it pleasurable	1	2	3	4	5	6	7	I don't find it pleasurable
* I am very absorbed in this activity	1	2	3	4	5	6	7	I am not at all absorbed in this activity
It's no fun at all	1	2	3	4	5	6	7	It's a lot of fun
* I find it energizing	1	2	3	4	5	6	7	I find it tiring
It makes me depressed	1	2	3	4	5	6	7	It makes me happy
* It's very pleasant	1	2	3	4	5	6	7	It's very unpleasant
* I feel good physically while doing it	1	2	3	4	5	6	7	I feel bad physically while doing it
* It's very invigorating	1	2	3	4	5	6	7	It's not at all invigorating
I am very frustrated by it	1	2	3	4	5	6	7	I am not at all frustrated by it
* It's very gratifying	1	2	3	4	5	6	7	It's not at all gratifying
* It's very exhilarating	1	2	3	4	5	6	7	It's not at all exhilarating
It's not at all stimulating	1	2	3	4	5	6	7	It's very stimulating
* It gives me a strong sense of accomplishment	1	2	3	4	5	6	7	It doesn't give me a strong sense of accomplishment
* It's very refreshing	1	2	3	4	5	6	7	It's not at all refreshing
I felt as though I would rather be doing something else	1	2	3	4	5	6	7	I felt as though there is nothing else I would rather be doing

* Denotes reversal when scoring.

APPENDIX K

DONUT MENU

Dunkin' Donuts Menu for Donut Study

Please choose 4 Donuts from each category:

Category 1 (<300 kcals)

Bavarian Kreme	Glazed	Vanilla Frosted
Chocolate Frosted	Jelly Filled	
Croissant Donut (CRONUT)	Strawberry Frosted	

Category 2 (300-400 kcals)

Boston Kreme	Chocolate Glazed Cake	Glazed Cake
Bow Tie	Cookie Dough	Maple Glazed
Brownie Batter	Double Chocolate Cake	Seasonal Donut (4th July, etc)
Chocolate Frosted Cake	Éclair	