PROLONGED IMPACT OF EXERCISE ON APPETITE AND ENERGY COMPENSATION

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ABSTRACT

Exercise generally leads to less than anticipated weight loss, despite inducing an acute negative energy balance. Post-exercise compensatory mechanisms that increase energy intake and decrease energy expenditure contribute to ineffective weight loss with exercise, although the precise mechanisms remain unclear. The aim of this thesis was to investigate the 3-day impact of exercise on measures of appetite and energy compensation in a healthy population of males and females. Fourteen participants completed two conditions in a randomized crossover trial: 1) 75 min exercise (75% VO_{2peak}); and 2) 75 min sedentary control. Measures of energy intake, energy expenditure, subjective appetite, and appetite-related hormones were assessed. An acute post-exercise suppression of acyl-ghrelin was observed. Exercise increased overall measures of subjective appetite despite no increase in energy intake or change in post-exercise physical activity patterns. Overall, exercise increased perceived appetite despite no clear evidence of energy compensation through energy intake or energy expenditure.

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STATEMENT OF CONTRIBUTIONS

This research was conducted within the Exercise and Nutrition Laboratory at the University of Lethbridge by Tetsuro Okada under the supervision of Dr. Marc Bomhof. Tetsuro Okada was the primary contributor to all efforts pertaining to the research and writing of all components presented in this thesis. The literature review, recruitment of participants, analysis of data, and writing of the paper was completed by Tetsuro Okada. Dr. Marc Bomhof conceptualized the original study design and obtained funding for the project.

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LIST OF ABBREVIATIONS

Symbol	Definition
AgRP	Agouti related peptide
ANOVA	Analysis of variance
ARC	Arcuate nucleus
AUC	Area under curve
BMI	Body mass index
CART	Cocaine- and amphetamine-regulated transcript
CCK	Cholecystokinin
CNS	Central nervous system
CSS	Composite satiety score
CVD	Cardiovascular disease
GAQ	Get Active Questionnaire
GLP-1	Glucagon-like peptide-1
HR	Heart rate
IL-6	Interleukin-6
MET	Metabolic equivalent of task
MICT	Moderate intensity continuous training
MRB	Meal-replacement beverage
NEAT	Non-exercise activity thermogenesis
NPY	Neuropeptide Y
PFC	Prospective food consumption
POMC	Pro-opiomelanocortin
PP	Pancreatic polypeptide
PYY	Peptide tyrosine tyrosine
SD	Standard deviation
SIT	Sprint interval training
TFEQ-R18	Three Factor Eating Questionnaire Revised 18-Item
VAS	Visual analogue scale
VO_{2max}	Maximal oxygen uptake
VO_{2peak}	Peak oxygen uptake
WC	Waist circumference
WHO	World Health Organization

CHAPTER 1: INTRODUCTION

The current and rising prevalence of obesity has become a global crisis (1, 2). Since 1975 to 2016, the World Health Organization (WHO) has reported that the prevalence of obesity around the world has nearly tripled from 4.7% to 13.1% (3). In 2016, approximately 67.5% of Canadians were classified as overweight and 29.4% as obese, suggesting that achieving and maintaining a healthy body weight has become a challenge for the majority of the population (3). Obesity is defined as a disease in which abnormal or excessive fat has accumulated to a degree that may present a health risk (4). While the underlying pathophysiology of obesity is complex, it can simply be stated that obesity is the result of a long-standing state of positive energy balance.

Energy balance, where body weight is maintained, is a state in which energy expenditure and energy intake are equal. A negative energy balance is induced through greater total energy expenditure than energy intake. Conversely, a positive energy balance results when more energy is consumed than energy expended from metabolic processes and physical activity. This energy surplus results in energy being stored within the body as adipose tissue through a process known as *de novo* lipogenesis (5). Other aspects influencing the etiology of obesity include genetic, sociocultural, behavioural, physiological, and environmental factors (6). Overweight and obesity are generally classified by body mass index (BMI), where a BMI of 25.0-29.9 $kg \cdot m^{-2}$ is considered overweight and $\geq$30.0 $kg \cdot m^{-2}$ is obese (1). Although BMI only accounts for the height and weight of an individual and does not account for body composition, research has demonstrated that a high BMI is associated with numerous diseases including cardiovascular disease (CVD) (7, 8), type 2 diabetes mellitus (9), certain cancers (10), obstructive sleep apnea (11), osteoarthritis (12, 13), non-alcoholic fatty liver disease (14), and kidney disease (15). Due to the metabolic comorbidities associated with increased BMI, various health organizations have

recommended increased levels of physical activity and exercise as a method to manage body weight (16-18).

Over the past decades, attempts at weight loss have increased, with 41.5% of the general population reporting trying to lose weight (19). Of these attempts at weight loss, 65.2% reported exercise as a strategy to increase energy expenditure and induce a negative energy balance (19). In addition to increasing energy expenditure, physical activity and exercise are associated with numerous health benefits, including the prevention of various chronic diseases and all-cause mortality (20, 21). The recommended levels of physical activity to achieve these health benefits include at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity aerobic physical activity per week (16, 22). Globally, 27.5% of adults do not meet the recommended physical activity guidelines (23). Additionally, 81% of adolescents between the ages of 11-17 around the world do not meet their daily, age specific physical activity guidelines of 60 minutes of moderate- to vigorous-intensity aerobic physical activity (22, 24). Within Canada, it is estimated that only 16% of adults over 18 years of age and 40% of children and youth aged 5-17 meet their respective physical activity guidelines (25, 26). The low frequency of physical activity globally and within Canada is troubling, as inadequate levels of physical activity and exercise are associated with CVD and other metabolic co-morbidities (27). Although there are a multitude of factors that contribute to reduced physical activity in our current environment, one factor that may play a role in the inadequate levels of physical activity is discouragement due to lower-than-expected levels of weight loss with exercise (28).

It has been reported that the majority of the population believes that exercise is an effective strategy for weight loss (28). Particularly in individuals with obesity, a belief that exercise helps with weight loss is one of the primary factors that leads to individuals becoming discouraged

from participating in regular physical activity (28). Despite the acute energy deficit associated with physical activity, exercise interventions are associated with only modest weight reduction. Using exercise as a method for weight loss remains a controversial topic (29).

Although exercise is generally regarded for its impact on the energy expenditure side of the energy balance equation, exercise has an equally important role on energy intake. In addition to increasing energy expenditure, exercise has been demonstrated to transiently suppress appetite during and immediately post-exercise (30). Further, exercise has been shown to induce short-term reductions in body weight (31, 32). However, despite the purported anorexigenic effects of exercise, reductions in body weight are often less than anticipated, where exercise results in little to no weight loss, or even weight gain (28, 33-36). These findings suggest that the acute energy deficit induced through a bout of exercise may be followed by some form of energy compensation.

Energy compensation refers to metabolic and behavioural adaptations in response to exercise-induced energy expenditure and/or caloric restriction in order to maintain body energy stores (37). Proposed mechanisms that play a role in energy compensation include increased appetite and energy intake (38, 39), a reduction of non-exercise activity thermogenesis (NEAT) (40-42), decreased resting metabolic rate (43, 44), increased efficiency of skeletal muscle (45, 46), and reduced adherence to prescribed exercise (33, 47, 48). The precise mechanisms for weight regain with exercise are not fully understood. It has been hypothesized that increased energy intake with exercise may be a primary contributor of energy compensation (38). However, studies investigating compensatory energy intake with a bout of exercise fail to demonstrate increased energy intake equaling exercise-induced energy expenditure (38, 49, 50). It is important to note that research investigating post-exercise energy intake and appetite-regulating hormones have

mainly focused on the 8-24 hr response following a bout of exercise (51, 52). Additionally, many short-term studies measuring energy intake utilize food journals or recalls, which are subject to error and have been demonstrated to underreport energy intake (53). Other studies that provide an *ad libitum* meal in a laboratory environment do not simulate real-life settings. The available literature examining post-exercise appetite and energy intake has yet to examine the prolonged response beyond the 24-hr period, leaving the potential for a delayed energy compensatory response following a bout of exercise. Understanding the energy compensatory mechanisms associated with exercise may provide individuals and health professionals with the knowledge to implement effective weight loss programs and prevent weight regain.

This thesis is comprised of five chapters. Chapter 1 provides a general introduction to the thesis. Chapter 2 contains a review of relevant literature regarding the neurobiology of appetite-related hormones and the compensatory responses due to exercise. The objectives and hypothesis of the thesis are also presented. Chapter 3 explains the methodology utilized for the thesis work. Chapter 4 presents the results from the data collected during the randomized crossover trial. Chapter 5 provides a discussion regarding the findings from the research, as well as the study strengths, limitations, overall conclusions, and future directions. All references are listed at the end of the thesis document.

CHAPTER 2: LITERATURE REVIEW

2.1 Neurobiology of Appetite Regulation

Exercise-induced energy compensation involves complex neurobiological pathways that regulate appetite-stimulating and appetite-suppressing hormones (54). In order to understand how exercise-induced fluctuations of appetite-related hormones impacts energy balance, it is important to recognize the physiological roles of various appetite hormones, how they are regulated, and how they influence energy intake.

2.1.1 Homeostatic System

The regulation of appetite and food intake involves a dynamic interaction between the homeostatic (metabolic) and hedonic (reward) systems. Homeostatic regulation refers to the human body constantly working to achieve a state of energy homeostasis, where long- and short-term energy intake is proportional to energy expenditure and energy stores are maintained (55, 56). The energy homeostasis system achieves a state of energy balance by utilizing short-term and long-term appetite-regulating hormones. Short-term, appetite-regulating hormones that have been studied include glucagon-like peptide-1 (GLP-1), peptide tyrosine tyrosine (PYY), cholecystokinin (CCK), pancreatic polypeptide (PP), and acyl-ghrelin. Of these hormones, GLP-1, PYY, CCK and PP induce feelings of satiety. The hormone acyl-ghrelin is the only known hormone to stimulate appetite (57). GLP-1 and PYY are released predominantly from endocrine L-cells from the ileum and colon (58-60). CCK is released mainly from I-cells within the duodenum and jejunum (61, 62) and PP is released from F cells within the islets of Langerhans of the pancreas (63). The short-term anorexigenic hormones play a role in the cessation of individual meals through increased perception of satiety, resulting from a transient rise of plasma

levels in GLP-1 (64, 65), PYY (60, 66-68), CCK (69, 70), and PP (63, 71), following the consumption of a meal. The hunger hormone, acyl-ghrelin, is primarily secreted from oxyntic glands within the stomach and is known for its role in meal initiation (72-74). Evidence supporting the physiological role of acyl-ghrelin was demonstrated by Cummings et al., investigating plasma acyl-ghrelin levels in humans throughout a 24 hr period (75). The results from the study demonstrated that circulating acyl-ghrelin levels rose an average of 78% prior to the onset of each meal (breakfast, lunch, and dinner) and subsequently decreased to or below baseline levels after meal termination (75). Furthermore, acyl-ghrelin concentrations were observed to be inversely associated with circulating levels of satiety hormones (75).

In addition to short-term appetite-regulating hormones, the homeostatic system utilizes long-term appetite-regulating hormones to maintain body energy stores, or 'set point'. Initially suggested by Kennedy (76) in 1953, set point theory revolves around the idea that each individual has a target 'set point' of body fat, that is regulated by a negative feedback system, now commonly referred to as 'lipostatic' regulation (56). Lipostatic regulation corrects for fluctuations in adipose tissue by sending signals to the brain to counteract these changes and consequently adjusts for energy intake and energy expenditure, proportionally. In healthy individuals, leptin, a hormone primarily secreted by adipose tissue, circulates the body in proportion to body fat and plays a role in energy regulation, metabolism, and immune function (55, 77). Similarly, insulin, a hormone produced by β-cells within the pancreas, circulates in proportion to adipose tissue and is released precisely to meet metabolic needs in healthy subjects (55, 78). However, leptin and insulin function may be impaired in individuals with obesity, resulting in leptin and insulin resistance (79). Both leptin and insulin are essential in the

regulation of long-term energy homeostasis by acting on receptors within the central nervous system (CNS) (80, 81).

Overall, both long- and short-term anorexigenic and orexigenic signals function to regulate appetite. The gut- and adipose-related appetite signals regulate appetite through stimulation or inhibition of various neurons within the hypothalamus of the forebrain and caudal brainstem of the hindbrain (55, 82). The arcuate nucleus (ARC) of the hypothalamus houses two subpopulations of neurons that co-express pro-opiomelanocortin (POMC)/cocaine- and amphetamine-regulated transcript (CART), and neuropeptide Y (NPY)/agouti related peptide (AgRP), which suppress and stimulate feeding, respectively (83). Appetite-regulating hormones work in conjunction with the CNS to regulate feelings of hunger and satiety from meal-to-meal. However, this diurnal pattern can be influenced through an acute bout of exercise, which has been shown to transiently reduce appetite.

2.1.2 Hedonic System

The second mechanism that contributes to appetite regulation is the hedonic system. The hedonic system represents the brain's food reward system, which is believed to be an evolutionary adaptation that promotes survival through behaviours such as binge eating and overconsumption of food beyond metabolic needs (82). The hedonic system is regulated similarly to the homeostatic system, through the CNS, however, is also influenced through external environmental factors such as sensory stimuli (i.e., visual, olfactory, auditory, taste), and availability, enjoyment, and palatability of food (84, 85). Despite evidence that the hedonic system encourages overfeeding, even while satiety hormones are present (82), Morton et al. (55) proposed that the food reward system is an essential component for energy homeostasis. This is

based on evidence from rodent models suggesting that satiety reduces the perception of food reward (86) and that food reward is increased through fasting or caloric restriction (55, 87, 88). This is supported by a study conducted in humans that observed increased levels of subjective appetite, food reward levels of 'liking' for high fat, sweetened foods, and energy intake following a 24-hr fast compared to a fed state (89). These findings from animal and human studies suggests an interaction between the hedonic system and fasting levels of leptin, insulin, and acyl-ghrelin to increase food reward and energy intake. While the homeostatic and hedonic systems differ, evidence suggests that they work in conjunction to achieve a state of energy balance (55, 85, 90).

2.2 Energy Compensation in Response to Exercise

2.2.1 Exercise and Appetite-Regulating Hormones

A considerable body of research has demonstrated that exercise has a profound impact on short-term, appetite-regulating hormones. Specifically, an acute bout of exercise has been shown to increase secretion of GLP-1 (91-96), PYY (91, 93, 94, 96, 97), CCK (98, 99), and PP (91, 100, 101), while simultaneously suppressing acyl-ghrelin (51, 52, 95, 97, 101-104). Douglas et al. investigated the acute effects of aerobic exercise on appetite regulation in males and females that were lean, overweight, and had obesity (93). Participants completed 60 min of running on a treadmill at 60% VO_2peak or a 60 min sedentary session. Appetite-regulating hormones were measured for 7 hours post-exercise and appetite perception was measured using a 100 mm visual analogue scale (VAS). Perceived appetite was lower in the exercise trial compared to control at 30, 60, and 90 minutes post-exercise. The overall appetite-suppressing effect of exercise was significantly greater in lean participants. These findings were reinforced through significant

elevations in total PYY and GLP-1 with exercise compared to the control trial. Additionally, there were group differences reported, with lower levels of total PYY and higher concentrations of GLP-1 in individuals with overweight/obesity compared to lean individuals following exercise. These findings suggest that participating in a bout of moderate-intensity aerobic exercise may acutely suppress perceived appetite through elevations in PYY and GLP-1 in both lean and overweight/obese individuals, with a greater magnitude of appetite suppression in lean individuals compared to individuals with overweight or obesity (93).

In another study, PYY and GLP-1 were also shown to significantly increase from baseline following moderate-intensity continuous exercise (MICT) and sprint interval exercise (SIT) on a cycle ergometer compared to a control trial (94). However, 90 min following the cessation of exercise, PYY and GLP-1 levels dropped below baseline. A decrease in perceived hunger was also observed following MICT and SIT trials. Furthermore, differences in sex were observed, with males exhibiting greater PYY post-exercise and a greater rise in GLP-1 in females immediately after exercise (94). In another study, Holliday & Blannin examined the impact of a 15, 30, and 45min bout of acute cycling at ~76% VO_2max in trained males. In the 30 min and 45 min, but not the 15 min, cycling trial, concentrations of GLP-1 were increased immediately following exercise (95). Acyl-ghrelin was also acutely suppressed across all three exercise trials, with the greatest decrease following 45 min of exercise. Conversely, there were no observed increases in PYY concentrations or subjective appetite between trials. Martins et al. conducted a study examining postprandial levels of appetite-related hormones and perceived appetite, using a VAS, following 60 min of cycling at 65% of estimated maximal heart rate (91). A significant decrease in perceived hunger and increase in blood PYY, GLP-1, and PP concentrations was

observed following an *ad libitum* meal, 1-hr post-exercise (91). Studies have also observed short-term elevated levels of CCK following a bout of exercise (98, 99).

Despite studies demonstrating a transient appetite-suppressing effect post-exercise, there are still inconsistencies between interventions. These may be due to various mechanisms that potentially impact circulating levels of appetite-regulating hormones following exercise. The purported mechanisms include redistribution of blood flow, alterations to the sympathetic nervous system, and elevations in interleukin-6 (IL-6), free fatty acids, glucose, and lactate with exercise (105). During a bout of exercise, the body redistributes blood flow from visceral organs to active skeletal muscle (106, 107). This redistribution of blood flow reduces the delivery of oxygen to the stomach, where ghrelin is mainly produced and secreted (73, 74). The decrease of blood flow to the stomach may explain reductions in plasma acyl-ghrelin following exercise (51, 105).

Exercise has also been shown to increase sympathetic nervous system activity (108). Increased stimulation of the sympathetic nervous system elevates concentrations of epinephrine and norepinephrine, which are negatively associated with circulating acyl-ghrelin (108, 109). Additionally, increased sympathetic nervous activity and catecholamines gives rise to circulating levels of GLP-1 and PYY (110, 111). Increased secretion of IL-6 from skeletal muscle during exercise has also been demonstrated to increase concentrations of GLP-1 in rodent models (112, 113). Elevated free fatty acid concentrations may inhibit secretion of ghrelin and concurrently stimulate the release of PYY, PP, and GLP-1 (114-116). High-intensity exercise has been shown to increase circulating concentrations glucose post-exercise, which may contribute to suppressed levels of ghrelin and increased GLP-1 (117-119). Furthermore, increased production of lactate from skeletal muscle during exercise is purported to play a role in suppressing the secretion of

ghrelin (105, 120). Other factors that may alter levels of appetite-regulating hormones following exercise involve individual differences, including BMI and sex, as well as the variations between the methodology of studies, such as exercise modality, intensity, and duration. Although the exact physiological mechanisms influencing exercise-induced change in appetite-regulating hormones are not fully understood, the general consensus in the literature is that exercise transiently reduces appetite (30, 102, 105).

2.2.2 Acute Impact of Exercise on Energy Intake

Exercise transiently reduces appetite through inhibition of acyl-ghrelin secretion and increased secretion of satiety hormones. Despite observed acute decreases in hunger and appetite, research examining acute, or same-day, energy intake following an exercise session is conflicting as studies have demonstrated no changes (52, 91, 93, 101, 121-125) and increases (126, 127) in energy intake with exercise. Balaguera-Cortes et al. investigated the effects of aerobic compared to resistance training on appetite and energy intake in a group of healthy, physically active males (101). As aerobic exercise expends more energy compared to resistance exercise of the same relative intensity, the study aimed to examine whether aerobic exercise results in higher levels of energy compensation. The results demonstrated no difference in energy intake between aerobic exercise, resistance training, or resting control trials. Although relative energy intake (exercise induced energy expenditure – energy intake) was not depicted in the results, the authors conclude that because aerobic exercise was estimated to expend more energy compared to resistance exercise, aerobic exercise elicits a greater acute energy deficit (101).

In another study, King et al. investigated the influence of aerobic exercise versus a control session on appetite and energy intake in a healthy, young male population (52). In the

randomized, crossover study, participants completed either a 90 min running session on a treadmill at ~70% VO_2max or a control session. *Ad libitum* meals were provided to participants at 1, 4, and 7.5 hrs post-session. There was a main effect of time for energy intake, with the highest energy consumed at 1 hr post-exercise. No differences in energy intake were observed between the exercise and resting trials, indicating that there was no energy compensation observed with exercise-induced energy expenditure(52). Consistent with this study, a study completed by Hagobian and colleagues observed no difference in absolute, post-exercise energy intake between an exercise and control trial in healthy males and females (124). However, a significant decrease in relative energy intake was demonstrated in both males and females when comparing the exercise to control trial. Similar findings were demonstrated in individuals with overweight/obesity, with no increase in absolute energy intake between exercise and control trials (93).

While the majority of studies have not observed acute energy compensation on the same day of exercise, there are some reports that contradict these findings. George & Morganstein demonstrated a significant increase in energy intake 1 hr post-exercise in females with overweight compared to normal weight females, following 1 hr of walking on the treadmill at 60% of maximum heart rate (HR) (127). The authors noted that this compensatory increase in energy intake may be attributed to higher energy requirements with the higher BMI in the overweight group. In another study conducted in active and inactive normal weight males, the exercise trial was found to have significantly higher energy compensation when compared to the control trial within the active group (126). Additionally, Pomerleau et al. investigated the effects of low- and high-intensity aerobic exercise on subsequent energy intake in young females. Post-exercise energy intake in the high-intensity exercise trial was demonstrated to be significantly

higher (128). However, relative energy intake was found to be lower after both exercise sessions compared to the control trial. Although the authors conclude that high-intensity aerobic exercise elicits higher energy intake in females, the results still demonstrate an acute energy deficit following exercise compared to a control trial (128).

Overall, studies investigating acute energy compensation following exercise have generally demonstrated both no change and increased absolute energy intake (52, 91, 93, 101, 121-127). These mixed findings may be due to various inter-individual and intervention differences, similar to the response of appetite-regulating hormones to exercise. Based on these studies, it is important to recognize the difference between absolute and relative measures of energy intake. Most studies report no differences in absolute energy intake when comparing different forms of exercise to resting control conditions. However, when taking into consideration the relative energy intake in acute energy compensation studies, they generally demonstrate an energy deficit on the same day of the exercise trial. This is supported by recent review articles demonstrating no acute energy compensation with exercise (38). However, due to inconsistencies between studies, it remains difficult to make conclusions about the short-term effects of exercise on energy intake (49).

2.2.3 Chronic Impact of Exercise on Energy Intake

Numerous studies have investigated the acute impact of exercise on subsequent energy intake, however, less is known about the prolonged and chronic effects of exercise on energy compensation beyond the 24-hour period. Recently, Martin et al. completed a 24 week randomized controlled trial in adults with overweight or obesity, comparing the effects of different intensities of exercise (expending 8 $kcal \cdot kg^{-1}$ of body $weight \cdot wk^{-1}$ (KKW) and 20

KKW) and no exercise on energy compensatory mechanisms (129). Given that energy intake equals energy expenditure in a weight stable individual, energy intake was measured using the doubly labelled water (DBL) technique. Furthermore, lunch and dinner food intake tests were completed >24 hrs after the last exercise session, at baseline and at 24 wk, and were measured following a standardized breakfast of a 190-kcal nutrition bar. Both meals consisted of *ad libitum* meals, which were weighed to calculate energy intake. The 8 and 20 KKW exercise groups were found to have compensated 76.3% and 90.2%, respectively, with significant differences between the groups (129). Change in energy intake was significantly different between the control and exercise groups. The control group had a reduction of 2.3 kcal/day in energy intake, whereas the 8 KKW and 20 KKW groups increased energy intake by 90.7 kcal/day and 123.6 kcal/day, respectively. No differences in energy intake were observed between the 8 and 20 KKW groups. These findings suggest that energy compensation occurs as a result of increased energy intake, due to exercise-induced energy expenditure (129).

The results of the aforementioned study coincide with other studies that utilize long-term exercise interventions (> 12 weeks) and increased exercise frequency (130, 131). Findings from a 12 wk intervention of aerobic exercise suggests that those who compensated, or had a lower than expected weight loss, may be doing so through an increase in energy intake (130). The authors also noted the importance of differentiating between compensators and non-compensators, as there is large individual variability in energy compensation (130). This is supported by evidence demonstrating that males who compensate have higher energy intake and lower NEAT, when compared to those who did not compensate and lost weight (132). Additionally, Church et al. conducted a 24 wk trial investigating energy compensation between 3 exercise groups: 4, 8, and 12 KKW, in sedentary postmenopausal females with overweight (131).

The study found that there was more compensation with increased exercise dose in the 12 KKW, however there were no differences in compensation between the 4 and 8 KKW groups (131).

Conversely, exercise intensity has been demonstrated to show no difference in weight loss and energy compensation in a 12 week endurance exercise intervention in overweight, sedentary males (133). Moderate- (~300 kcal·day^{-1}) and high-doses (~600 kcal·day^{-1}) of endurance exercise resulted in no differences in loss of fat mass and no changes in energy intake throughout the intervention (133). Overall, these findings are consistent with the systematic review conducted by Riou et al. which found that longer-term exercise interventions are associated with energy compensation approaching ~84% of exercise-induced energy expenditure (38).

2.2.4 Exercise and Non-Exercise Activity Thermogenesis (NEAT)

In addition to the transient satiety-inducing impact of exercise, it is important to consider the subsequent non-structured physical activity or NEAT associated with exercise. It has been postulated that following a bout of structured physical activity, such as aerobic and resistance training, the body compensates for the exercise-induced energy expenditure by reducing NEAT (33, 38, 134). This has been demonstrated in a study investigating energy compensation with exercise in healthy males and females with overweight/obesity, over a 10-month period (132). Seventeen males from the study, who were categorized as non-responders (failed to lose 5% or more of their baseline body weight in response exercise-induced energy expenditure) were found to have decreased levels of non-exercise energy expenditure, or NEAT. NEAT was assessed using an accelerometer worn around the waist for 7 consecutive days. Although Herrmann et al. did not observe any changes in post-exercise NEAT in female participants (132), Colley et al. demonstrated a compensatory response in females with obesity, where a significant decrease in

NEAT was reported following an exercise intervention (40). Similarly, a recent study by Riou et al. demonstrated decreased NEAT in twenty-five premenopausal females with overweight/obesity, following an exercise intervention at low intensity (40% of VO_2reserve) and moderate intensity (60% of the VO_2reserve) (42). The experiment was a total of four months in length, with the first month including no exercise, and the subsequent three months involving exercise interventions. Measurements of NEAT were collected using two triaxial accelerometers around the arm and thigh and were observed at 3 phases: at baseline (7 days), week 1 post-initiation of exercise (14 days), and week 12 of the exercise intervention (7 days). NEAT was significantly reduced at week 1 and week 12 in both exercise intervention groups in relation to baseline NEAT. The findings from this study demonstrate energy compensation by decreasing NEAT in response to increased structured physical activity (42).

Conversely, studies have demonstrated no compensatory changes in NEAT following exercise interventions (135-138). A study done in 2008 found no decreases in NEAT following moderate- and high-intensity aerobic exercise interventions in lean males and females (137). Furthermore, Willis et al. observed no decreases in NEAT following a 10-month aerobic training program in sedentary young adults with overweight/obesity (138). This finding is supported by a recent study conducted by Myers et al. demonstrating no compensatory changes in NEAT in response to a structured, aerobic exercise intervention in females with overweight (139).

Similar to the acute appetite suppression associated with exercise, research examining post-exercise NEAT is conflicting due to large individual variation, as well as differences in study interventions. Post-exercise NEAT may be influenced by exercise duration and the age and sex of the research participants (140). Although there is mixed evidence, systematic reviews purport that there is no clear evidence of compensatory reductions in NEAT following exercise (41,

140). Future research examining energy compensation with exercise should include measures of NEAT and total energy expenditure to determine relative measures of energy compensation with exercise-induced energy expenditure.

2.3 Rationale for Study

The challenges associated with achieving long-term weight loss with exercise are evident with sustained and global increases in obesity. Exercise does not typically elicit an energy compensatory response on the same day that the exercise is performed, resulting in a short-term energy deficit. Whereas longer-term interventions report some compensation through increased energy intake or energy expenditure. Overall, there is a lower amount of weight loss than predicted from exercise-induced energy expenditure. Research to date has not adequately assessed appetite, energy intake, and energy compensation beyond the 24-hr, post-exercise period. Many short-term studies measuring energy intake utilize food journals or recalls, which have been demonstrated to underreport energy intake. Other studies that provide an *ad libitum* meal in a laboratory environment do not simulate real-life settings. Therefore, there is still potential for a prolonged (24-72 hrs) energy compensatory response following a bout of aerobic exercise. Determining how exercise impacts both the energy expenditure and energy intake sides of the energy balance equation over a period of time greater than 24 hrs may provide a better understanding as to why weight loss with exercise is generally less than expected.

2.4 Objective and Hypothesis

The objective of this study was to determine the prolonged effect of a single session of aerobic exercise on subjective levels of appetite, appetite-related gut hormones, and energy compensation in healthy, weight-stable males and females. Specifically, our goal was to

determine whether a bout of aerobic exercise would stimulate compensatory responses through increases in energy intake or decreases in NEAT over a 72-hr period. Secondary outcome measures included assessment of perceived appetite and circulating levels of acyl-ghrelin, GLP-1, and PYY. This study aimed to provide a novel approach to accurately measure energy intake in a real-world setting through the use of a standardized meal-replacement-beverage (MRB) diet of Ensure®Plus. Based on previous literature, we hypothesized that exercise would promote greater energy compensation through increases in energy intake relative to a reduction in NEAT. Additionally, due to the energy compensation, we predicted that there would be no differences in subjective appetite or in levels of acyl-ghrelin, GLP-1, and PYY.

CHAPTER 3: MATERIALS AND METHODS

3.1 Participants

Fourteen participants (6 female; 8 male) volunteered to take part in a randomized, counterbalanced crossover trial. Participants were recruited from the University of Lethbridge and surrounding area through posters, advertisements on social media, and word of mouth. Participants were healthy (no history of serious physical injuries or metabolic disease), self-reported weight stable, not actively attempting to lose or gain weight, and were not restricted eaters. Additional exclusion criteria included taking medications that could influence appetite, smokers, and if a participant had initiated a new form of contraceptive within the previous three months. Participants provided written informed consent prior to taking part in the study. The study was approved by the University of Lethbridge Human Participant Research Committee (Ethics ID #2020-058) and was conducted in accordance with the ethical principles of the *Declaration of Helsinki.*

3.2 Preliminary Session and Test Trial

Prior to baseline testing, participants reported to the lab for an initial screening session and subsequently completed a test trial. Participants completed the Get Active Questionnaire (GAQ; Appendix A) to screen for contraindications to the exercise protocol (141). Restrained eating was assessed using the Three-Factor Eating Questionnaire Revised 18-item (TFEQ-R18; Appendix B) consisting of 6 questions on a response scale from 1-4 (142, 143). Individuals that scored ≥ 18 on the restrained eating subscale were classified as restrained eaters and were excluded from the study (144). Participants interested in the study were initially provided with an introduction to

the research project where they completed a health screening form (Appendix C), physical activity questionnaire (145) (Appendix D) and provided written informed consent (Appendix E).

Following the initial screening session, participants were asked to complete a test trial in order to test an individual's ability to tolerate a liquid diet to reduce potential dropout from the study. For the test trial, 6 bottles of a liquid MRB beverage (Ensure®Plus, Abbott Laboratories, Chicago, IL, USA) were provided to participants in a variety of flavours (chocolate, vanilla, and strawberry). With the exception of water, participants were asked to exclusively consume the provided Ensure®Plus, starting with the first meal of the day and continue *ad libitum* consumption until the end of the day or until the MRB drinks were all consumed to assess whether they were able to tolerate and adhere to exclusive consumption of Ensure®Plus over a 4-day period. In addition to the MRB, participants were provided with a single daily fibre bar (NuGo Fiber d'Lish, NuGo Nutrition, Oakmont, PA, USA), to provide adequate daily intake of fibre. Participants that were able to tolerate the test trial and willing to participate in the study moved on to complete baseline testing.

3.3 Baseline Testing

Participants recruited for the study completed a baseline session that included measures of height, weight, and performed a VO_{2peak} test (ml $O_2 \cdot kg^{-1} \cdot min^{-1}$). VO_{2peak} refers to the highest volume of oxygen that was measured for an individual during an incremental exercise test (146). VO_{2peak} was assessed using an incremental ramp test on a motorized treadmill, based on the modified Astrand protocol (147, 148). Participants initially completed a 5-minute warm-up on a motor-driven treadmill with a speed between 5.6-8.9 $km \cdot h^{-1}$ at 0% grade. Following warm-up, the speed of the treadmill was increased every minute by 0.8 $km \cdot h^{-1}$ until a speed of 9.7-12.9

$km \cdot h^{-1}$ was achieved, depending on the fitness level of the participant. Once the goal speed was achieved, the grade of the treadmill was increased by 2% every 2 min. Participants continued running until voluntary exhaustion. Following termination of the incremental test, participants were required to perform a minimum 3 min cool-down of walking on the treadmill at a self-selected pace. All participants received similar strong verbal encouragement from the researcher throughout the incremental test. Oxygen consumption and respiratory exchange ratio was continuously measured using indirect calorimetry (COSMED, Concord, CA, USA), and heart rate was monitored via a heartrate monitor (Garmin, Olathe, KS, USA). Height and weight were recorded to the nearest 0.1 cm and 0.1 kg, respectively, on a calibrated Health-o-meter® professional weighing scale (Pelstar® LLC, McCook, IL, USA). Baseline testing took approximately 60 min to complete.

3.4 Experimental Sessions

At least 3-days following baseline testing, participants completed two, 4-day crossover trials: 1) sedentary control (75 min sedentary activity) and 2) exercise (75 min of aerobic exercise performed at 75% VO_{2peak} on a motorized treadmill) in a randomized, counterbalanced order (Figure 3.4). Trials were scheduled a minimum 1 week apart for males and 4 weeks apart for females, within the early follicular phase of the menstrual cycle (day 1-10), to control for potential appetite fluctuations (149-151).

For each trial, participants were required to exclusively consume a standardized MRB (Ensure®Plus) to minimize the inaccuracy of energy intake measurements. The Ensure®Plus MRB provides participants with complete, balanced nutrition (Calories = 350 kcals; Total fat =

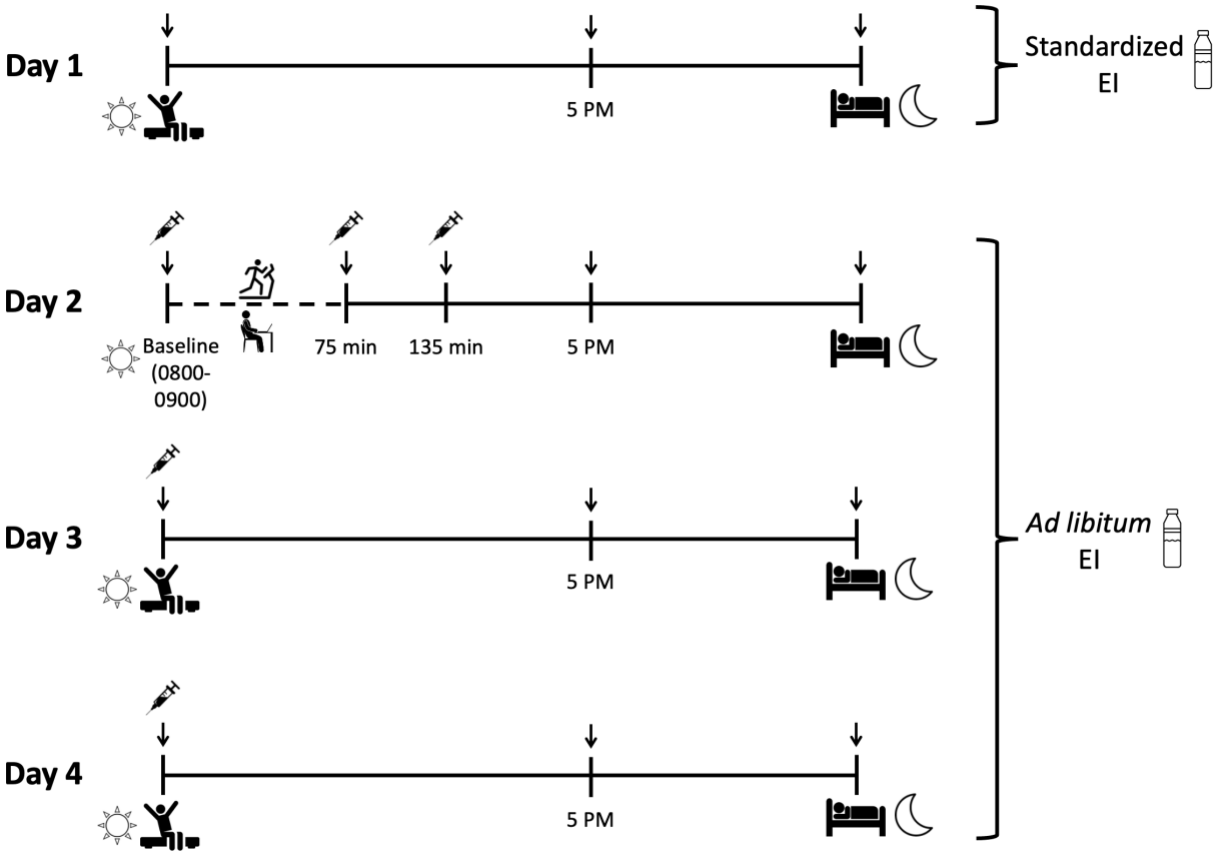

Figure 3.1 **Timeline of experimental conditions**
Participants arrived at the laboratory in the morning (0800-0900) in a fasted state (>10 hrs).
↓ Appetite visual analogue scale; 💉 blood sample; --- 75 min of exercise or sedentary condition.

11 g [Saturated fat = 1.5 g; Polyunsaturated fat = 4 g; Monounsaturated fat = 5 g]; Total carbohydrate = 48 g [Dietary fibre 1 g; Total sugars = 22 g; Added sugars = 21 g]; Protein = 16 g) (152). The labels on the Ensure®Plus were removed, with each bottle only indicating the flavour in order to blind participants to the brand and energy content of the standardized MRBs.

Prior to each session, participants were asked to refrain from strenuous exercise, alcoholic and caffeinated beverages in the 24 hrs leading into the trial. On day 1 of the first randomized trial, participants were provided excess MRB and asked to consume the drinks *ad libitum*. To standardize the energy intake prior to the day exercise or sedentary conditions would be completed (day 2) for the second trial, participants were provided the same amount of energy

they consumed on day 1 for the first trial. On day 2 of each trial, participants reported to the Exercise and Nutrition Laboratory (PE248) at the University of Lethbridge at 0800-0900hr following an overnight fast (>10 hrs). Fasting was verbally confirmed in the morning. A fasting blood collection via venipuncture was obtained, and participants completed the 75 min session of sedentary control or 75 min of aerobic exercise at 75% VO_{2peak}. Additional blood was collected immediately following the cessation of exercise or sedentary control and 1 hr post-exercise/sedentary conditions. After completing the exercise or sedentary condition (~135 min) participants were free to leave the laboratory and begin *ad libitum* intake of Ensure®Plus and water.

For days 2 to 4 of each trial, participants were provided a surplus of Ensure®Plus to make sure participants had an adequate supply of energy for each day. On days 3 and 4 of each trial, participants reported to the laboratory in the morning at 0800-0900hr following an overnight fast (> 10 hrs) to return all empty, partially empty, and full bottles of Ensure®Plus to confirm energy intake. Additional fasted blood draws were taken in the morning on days 3 and 4 of each trial, and participants were provided with a surplus of Ensure®Plus and instructed to continue *ad libitum* consumption of Ensure®Plus and water. To assure that participants received sufficient dietary fiber, participants were provided with a daily fibre bar (Calories = 150 kcals; Total fat = 3 g; Total carbohydrate = 31 g [Dietary fibre = 12 g; Total sugars = 10 g; Added sugars = 8 g]; Protein = 3 g) (NuGo Fiber d'Lish, NuGo Nutrition, Oakmont, PA, USA) for each 4-day trial.

Throughout each trial, participants were permitted to consume coffee and tea products on the condition that they contained no additives (e.g., cream and sugar. Participants were requested to keep track of caffeinated beverages consumed for each day of the first trial. For each day of the second trial, participants were asked to consume an equal volume of caffeinated beverages that

was recorded on each day of the first trial (i.e., if a participant drank one 250 mL cup of coffee/day during days 1-4 of the first trial, that participant was asked to consume one 250 mL cup of coffee/day during days 1-4 of the second trial).

For day 1-4 of each trial, participants completed a visual analogue scale (VAS) (153) to assess subjective measures of hunger, satisfaction, prospective food consumption (PFC), and fullness. VAS were completed through days 1-4 of both trials when participants woke up, around dinner time (~1700hr) and before they went to sleep. Additional VAS were completed on day 2 of each trial immediately after and 1 hr following exercise and sedentary conditions. An additional measure of subjective appetite was calculated by taking the mean appetite rating using the 4 measures of appetite from the VAS (hunger, satisfaction, fullness, and PFC) through the composite satiety score (CSS) (154). CSS was calculated using the equation: CSS (mm) = (satisfaction + fullness + (100 – PFC) + (100 – hunger))/4 (155). Previous studies have utilized the CSS (154-157) as it provides a mean appetite rating of the 4 subjective measures of hunger, satisfaction, fullness, and PFC.

Participants were also asked to wear an activity tracking monitor (activPAL4™) throughout day 1-4 of each trial to measure potential changes in daily activity levels, sedentary behaviour, and estimate measures of energy expenditure. The total time commitment for each participant was estimated to be ~10 hrs dedicated within the Exercise and Nutrition Laboratory, and a total of 8 days on the liquid MRB diet, over a 2-6 week period for this study. Participants were provided with the $50 upon the completion of each 4-day trial.

3.5 Measurement of Activity Level

Baseline levels of physical activity were measured using Godin's leisure time exercise questionnaire (145). An overall weekly mean Metabolic Equivalent of Task (MET)·hours was determined by multiplying the number of weekly hours each participant spent in mild (e.g., easy walking), moderate (e.g., fast walking), and vigorous physical activity (e.g., running) by an estimated value of 3 MET·h, 5 MET·h, and 9 MET·h, respectively.

Activity level was measured with an activPAL4™ (PAL Technologies Ltd, Scotland, UK) inclinometer. The activPAL4™ device was enclosed in a nitrile sleeve and secured to the thigh using medical tape. Skin was monitored daily throughout each 4-day trial period. To reduce skin irritation, the activPAL4™ device were wrapped in a finger cot after the nitrile sleeve. Both the finger cots and the nitrile sleeves were single use. The activPAL4™ inclinometers are only 9 grams and 5mm thick, making them comfortable for 4-day placement on the thigh. The activPAL4™ software classifies an individual's free-living activity into periods spent sleeping, lying, sitting, standing and ambulating, as well as step counts, providing accurate measurement and quantification of these movement behaviours over each 4-day trial. Additionally, the activPAL4™ assessed measures of energy expenditure as MET values. In order to obtain energy expenditure as kcal values, daily MET values were multiplied by estimated basal metabolic rate using the Harris-Benedict equation (male: (66.5)+(13.7·weight in kg)+(5·height in cm)-(6.8·age in years); female: (655)+(9.6·weight in kg)+(1.8·height in cm)-(4.7·age in years)) (158).

Energy balance was determined to assess whether each participant was in a state of negative, neutral, or positive energy balance and was calculated using the following equation: Energy balance = total energy intake – total energy expenditure.

3.6 Phlebotomy

Venipuncture was performed by a trained phlebotomist, using a vacutainer or syringe and 21-gauge needle. The phlebotomist wore the appropriate personal protective equipment including gloves, lab coat, mask, and eye protection. With the participant lying in supine position, the veins were assessed at the antecubital fossa of the arm after applying a tourniquet. Once an appropriate vein had been identified, the tourniquet was removed, and the site was cleaned with a 70% isopropyl alcohol swab. The tourniquet was reapplied after the site has dried and blood was drawn from the area in a previously chosen antecubital vein. For each blood draw, 6 mL was collected. Once the blood draw had finished (or terminated by the participant due to syncope, pain, or no longer wanting to continue), the tourniquet was removed prior to removing the needle. Gauze was placed over the puncture site and the participant was asked to place pressure on it. After checking to ensure that a clot was beginning to form, a piece of tape was placed over the gauze and participants were told to refrain from lifting any heavy objects for at least 1 hour. Needles were discarded into a sharps container that were disposed of as per biohazard protocols at the University of Lethbridge

3.7 Biological Analysis of Satiety Hormones

All blood samples were collected into pre-cooled 6 mL K_2Ethylenediaminetetraacetic acid spray-coated vacutainers (BD, Mississauga, ON, Canada). Immediately after collection, a protease inhibitor cocktail containing dipeptidyl peptidase IV inhibitor (10ul/ml blood; MilliporeSigma Corp., ON, Canada), sigma protease inhibitor (1mg/ml blood; SigmaFast, MilliporeSigma Corp.) and pefabloc (1mg/ml blood; MilliporeSigma Corp.) was added to the sample to prevent degradation of appetite-related hormones. Blood samples were centrifuged at

2500g for 10-minutes at 4°C. Plasma aliquots were stored at -80°C for later analysis.The concentration of PYY was determined using the Human PYY (Total) ELISA kit (MilliporeSigma Corp.). GLP-1 concentration was assessed using the High Sensitivity GLP-1 Active Chemiluminescent ELISA kit (MilliporeSigma Corp.). Acyl-ghrelin concentration was assessed by the Human Ghrelin (Active) kit (MilliporeSigma Corp). All samples were assayed in duplicate. The intra- and inter-assay variation for these assays ranged between 2-7% in our laboratory, as previously described (159).

3.8 Statistical Analysis

SPSS software v26.0 for Windows was used to analyze the data. Our primary outcome measure was determination of energy intake between the exercise and sedentary trials. Sample size estimations were completed using G*Power ($\alpha = 5\%$, $\beta = 80\%$) using an effect size of 1.20 and the analysis of variance (ANOVA): repeated measures, within factors statistical test. The effect size was based a previously conducted pilot study investigating the impact of exercise on energy intake utilizing a similar randomized crossover study design and MRB to measure energy intake. Data was assessed for normality using the Shapiro-Wilk test. Differences in acyl-ghrelin, GLP-1, PYY, subjective appetite, energy intake, energy expenditure, and energy balance were analyzed using a two-way repeated measures ANOVA. If a significant condition x time interaction was observed, post-hoc least significant difference pairwise comparisons were used to determine between condition differences. Within-condition differences were examined using a one-way repeated measures ANOVA. Effect size for repeated measures ANOVA was determined using partial eta squared (η^2), while effect size for post-hoc pairwise comparisons was calculated using Cohen's *d*. The magnitude of effect size was determined by the following

criteria: small ($\eta^2 = 0.01$; $d = 0.2$), medium ($\eta^2 = 0.06$; $d = 0.5$), and large ($\eta^2 = 0.14$; $d = 0.8$). Area under the curve (AUC) was assessed for appetite-related hormones and perceived appetite. AUC estimations were calculated using trapezoidal sums. Statistical significance was set at $P < 0.05$. All data is represented as mean ± standard deviation (SD).

CHAPTER 4: RESULTS

4.1 Participants and Baseline Measurements

A total of 26 participants were initially recruited for the study. Two participants were excluded from the study due to restrained eating. Additionally, a participant was excluded from the study due to a prescribed medication that potentially impacted appetite. Twenty-three participants completed the test trial phase of the study, with 9 participants reporting that they could not tolerate an exclusive MRB diet for 4 consecutive days. No participants dropped out of the study following the test trial, leaving 14 participants (6 female, 8 male) that completed the study. Participants had an average (mean ± SD) age of 23.6 ±3.4 years, BMI of 24.7 ± 3.6 $kg \cdot m^{-2}$, WC of 83.5 ± 7.6 cm, $MET \cdot h \cdot wk^{-1}$ of 43.9 ± 30.1, and VO_{2peak} of 41.5 ± 4.8 ml $O_2 \cdot kg^{-1} \cdot min^{-1}$ (Table 1). Participants had a mean restrained eating score of 13.0 ± 3.1. Female participants began the 4-day trial on day 5.5 ± 1.4 (exercise = 5.0 ± 1.4; sedentary = 6.0 ± 1.4) of the menstrual cycle.

Table 4.1 **Participant demographics**
Mean ± SD (range)

	Total (*n* = 14)	Females (*n* = 6)	Males (*n* = 8)
Age (years)	23.6 ± 3.4 (18 – 31)	23.0 ± 3.5 (18 – 27)	24.0 ± 3.5 (20 – 31)
Height (m)	1.7 ± 0.1 (1.6 – 1.8)	1.7 ± 0.1 (1.6 – 1.8)	1.8 ± 0.1 (1.6 – 1.8)
Weight (kg)	73.8 ± 14.2 (50.8 – 98.8)	62.7 ± 9.8 (50.8 – 78.2)	82.2 ± 11.0 (67.0 – 98.8)
BMI ($kg \cdot m^{-1}$)	24.7 ± 3.6 (17.1 – 29.9)	22.7 ± 4.0 (17.1 – 28.7)	26.3 ± 2.5 (22.3 – 30.0)
WC (cm)	83.5 ± 7.6 (71.7 – 96.0)	78.8 ± 6.9 (71.7 – 90.1)	87.1 ± 6.4 (77.7 – 96.0)
$MET \cdot h \cdot wk^{-1}$	43.9 ± 30.1 (3.0 – 89.0)	43.3 ± 26.3 (6.8 – 86.0)	44.8 ± 33.8 (3.0 – 89.0)
VO_{2peak} ($ml\ O_2 \cdot kg^{-1} \cdot min^{-1}$)	41.5 ± 4.8 (35.4 – 50.5)	41.0 ±6.2 (35.4 – 50.5)	41.8 ± 3.9 (36.0 – 45.7)

4.2 Perceived Appetite

Measures of perceived hunger, satisfaction, fullness, and PFC were measured at 14 time points (Day 1, 3, & 4: [morning after waking up, evening ~1700, and before bed]; Day 2: [morning after waking up, immediately post-exercise/sedentary, 1 hr post-exercise/sedentary, evening ~1700, and before bed]). No condition x time interactions were observed for any measures of subjective appetite (hunger, $P = 0.859$, $\eta^2 = 0.03$; satisfaction, $P = 0.996$, $\eta^2 = 0.02$; fullness, $P = 0.297$, $\eta^2 = 0.09$; PFC, $P = 0.120$, $\eta^2 = 0.10$) (Figure 4.1A). There was a main effect of time for perceived hunger ($P = 0.025$; $\eta^2 = 0.20$), satisfaction ($P < 0.001$; $\eta^2 = 0.21$), and fullness ($P = 0.012$; $\eta^2 = 0.22$), but not PFC ($P = 0.061$; $\eta^2 = 0.16$). A main effect of condition was observed for perceived fullness ($P = 0.027$; $\eta^2 = 0.32$) and PFC ($P = 0.025$; $\eta^2 = 0.33$), but not for hunger ($P = 0.105$; $\eta^2 = 0.19$) or satisfaction ($P = 0.060$; $\eta^2 = 0.25$). AUC differences were observed between the exercise and sedentary conditions for fullness ($P = 0.044$; $d = 0.60$) and PFC ($P = 0.014$; $d = 0.76$), where participants were less full and felt like they could eat more during the exercise condition. No AUC differences between conditions were observed for hunger ($P = 0.098$; $d = 0.48$) or satisfaction ($P = 0.088$; $d = 0.49$). Overall, for the CSS, there was a main effect of condition ($P = 0.020$; $\eta^2 = 0.35$) and time ($P = 0.023$; $\eta^2 = 0.21$), but no condition x time interaction effect ($P = 0.798$; $\eta^2 = 0.05$) was observed (Figure 4.2A). The AUC for CSS was greater for exercise compared to the sedentary condition ($P = 0.021$; $d = 0.70$).

4.3 Appetite-Related Hormones

4.3.1 Acyl-Ghrelin

A condition x time interaction ($P < 0.001$; $\eta^2 = 0.38$) and main effect of time ($P = 0.008$; $\eta^2 = 0.23$) was observed for fasted concentrations of acyl-ghrelin (Figure 4.3A). No main effect of

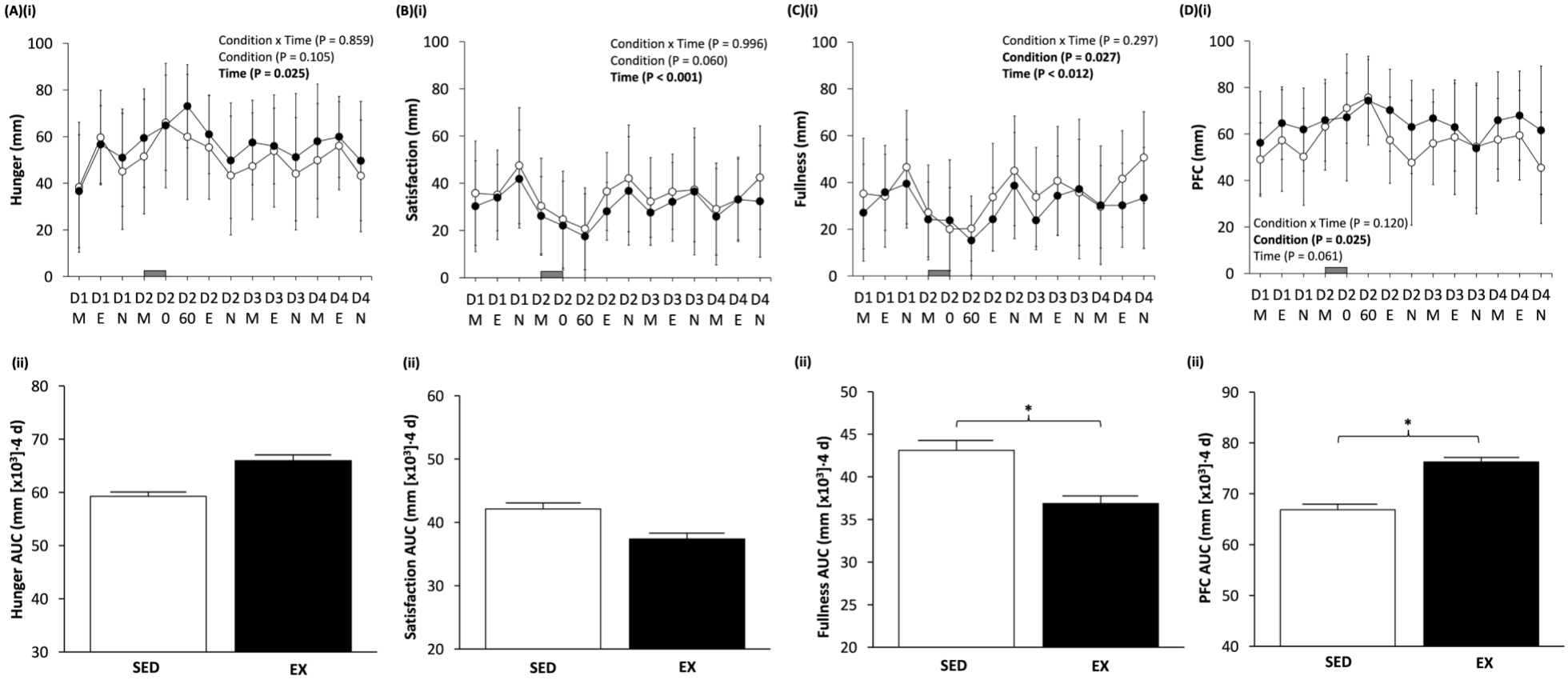

Figure 4.1 **Subjective measures of appetite**

Measures of perceived appetite of **(A)** hunger, **(B)** satisfaction, **(C)** fullness, and **(D)** PFC on a (*i*) 100 mm VAS [D_, day 1, 2, 3, or 4; M, morning; E, evening; N, night; 0, immediately post-EX/SED; 60, 60-min post-EX/SED] and (*ii*) total AUC between SED and EX conditions. Open circles display the SD condition. Filled circles display the EX condition. The grey shaded rectangle illustrates 75 min of EX or SED. Values are means ± SD, n=14. **P*<0.05 between SED and EX. PFC, prospective food consumption; VAS, visual analogue scale; SED, sedentary; EX, exercise.

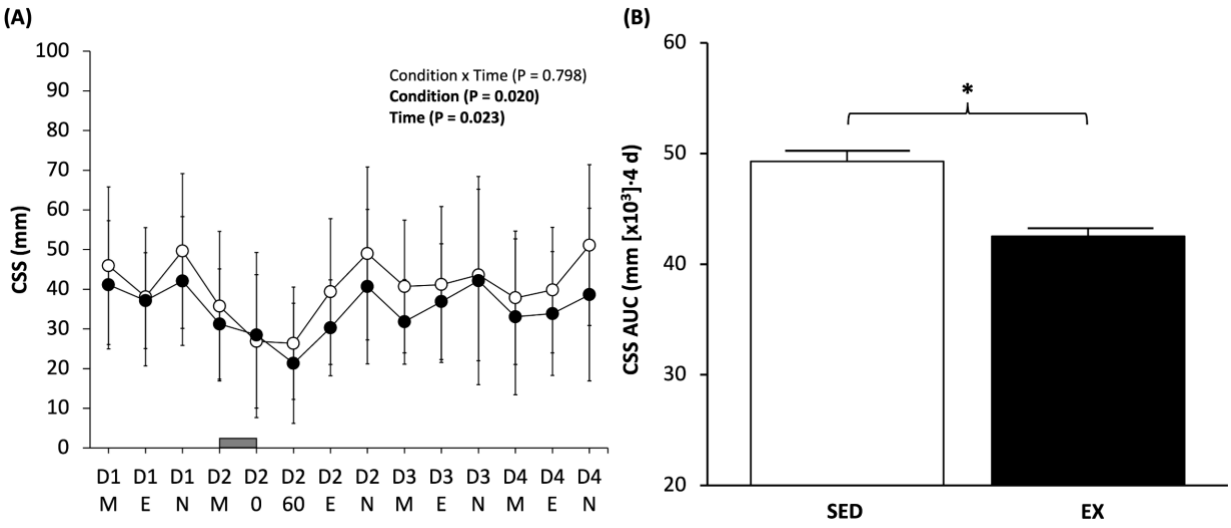

Figure 4.2 **Composite satiety score**
Mean appetite rating of subjective appetite based on: (*i*) a 100 mm VAS [D_, day 1, 2, 3, or 4; M, morning; E, evening; N, night; 0, immediately post-EX/SED; 60, 60-min post-EX/SED] and (*ii*) total AUC between SED and EX conditions. Open circles display the SD condition, while filled circles display the EX condition. The grey shaded rectangle illustrates 75 min of EX or SED. Values are means ± SD, n=14. **P*<0.05 between SED and EX. CSS, composite satiety score; VAS, visual analogue scale; SED, sedentary; EX, exercise.

condition ($P = 0.087$; $\eta^2 = 0.21$) was observed. *Post-hoc* pairwise comparisons demonstrated lower levels of acyl-ghrelin during the exercise condition immediately post-exercise ($P = 0.004$; $d = 0.92$) and 60 min post-exercise ($P = 0.022$; $d = 0.69$), compared to the sedentary condition. There were no differences in fasted acyl-ghrelin concentrations at baseline prior to the initiation of the exercise and sedentary conditions ($P = 0.575$; $d = 0.15$), day 3 ($P = 0.778$; $d = 0.08$), and day 4 ($P = 0.309$; $d = 0.28$). Within-condition, fasted concentrations of acyl-ghrelin were reduced immediately post-exercise ($P = 0.004$) in the exercise condition. In the sedentary condition, within-condition levels of acyl-ghrelin significantly increased 60 min post-sedentary ($P = 0.004$), relative to baseline. No differences in AUC for fasted concentrations of acyl-ghrelin were observed over each 4-day trial ($P = 0.507$; $d = 0.18$).

4.3.2 Glucagon-Like Peptide-1 (GLP-1)

No significant condition x time interaction ($P = 0.734$; $\eta^2 = 0.02$), main effect of condition ($P = 0.569$; $\eta^2 = 0.03$), or main effect of time ($P = 0.514$; $\eta^2 = 0.03$) was observed for fasted levels of GLP-1 (Figure 4.3B). Concentrations of GLP-1 did not differ at baseline ($P = 0.739$; $d = 0.09$), immediately post-exercise/sedentary ($P = 0.508$; $d = 0.18$), 1-hr post-exercise/sedentary ($P = 0.338$; $d = 0.27$), day 3 ($P = 0.707$; $d = 0.10$), and day 4 ($P = 0.926$; $d = 0.03$). No AUC differences were observed between conditions for GLP-1 ($P = 707$; $d = 0.10$).

4.3.3 Peptide Tyrosine Tyrosine (PYY)

There was no observed condition x time interaction ($P = 0.226$; $\eta^2 = 0.12$), main effect of condition ($P = 0.133$; $\eta^2 = 0.17$), or main effect of time ($P = 0.132$; $\eta^2 = 0.13$) for fasted concentrations of total PYY (Figure 4.3C). There were no differences in fasted concentration of PYY at baseline ($P = 0.866$; $d = 0.05$), immediately post-exercise/sedentary ($P = 0.091$; $d = 0.49$), 1-hr post-exercise/sedentary ($P = 0.153$; $d = 0.41$), day 3 ($P = 0.488$; $d = 0.19$), or day 4 ($P = 0.708$; $d = 0.10$). Within-condition, fasted levels of PYY were significantly reduced immediately post-sedentary ($P = 0.026$), and 1-hr post-sedentary ($P = 0.034$), relative to baseline. No differences in AUC were observed for AUC PYY ($P = 0.219$; $d = 0.34$).

4.4 Energy Intake

There was no significant condition x time interaction ($P = 0.704$; $\eta^2 = 0.04$), main effect of condition ($P = 0.390$; $\eta^2 = 0.06$), or main effect of time ($P = 0.407$; $\eta^2 = 0.07$) for energy intake throughout the trials (Figure 4.4). No differences in total energy intake ($P = 0.401$; $d = 0.23$) and daily energy intake (Day 1: $P = 0.336$, $d = 0.27$; Day 2: $P = 0.352$, $d = 0.26$; Day 3: $P =$

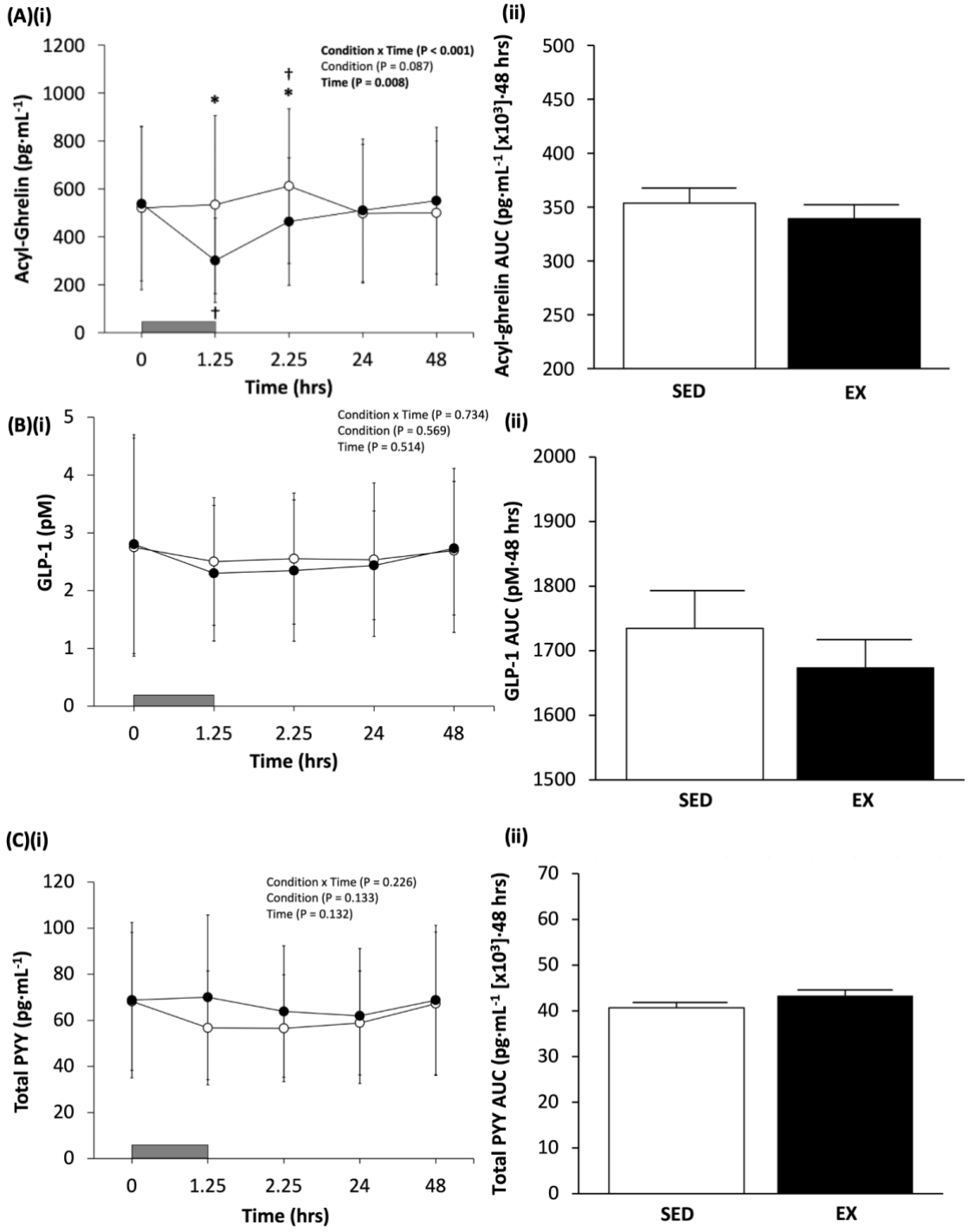

Figure 4.3 **Measures of appetite-related hormones**
(*i*) Concentrations and (*ii*) total AUC measures of **(A)** acyl-ghrelin, **(B)** GLP-1, and **(C)** total PYY between SED and EX condition. Open circles display the SD condition. Filled circles display the EX condition. The grey shaded rectangle illustrates 75 min of EX or SED. Values are means ± SD, n=14. **P*<0.05 between SED and EX. †*P*<0.05 EX within-condition relative to baseline. GLP-1, glucagon-like peptide 1; PYY, peptide tyrosine tyrosine; SED, sedentary; EX, exercise.

0.629, d = 0.13; Day 4: P = 0.342, d = 0.26) were observed between the exercise and sedentary conditions.

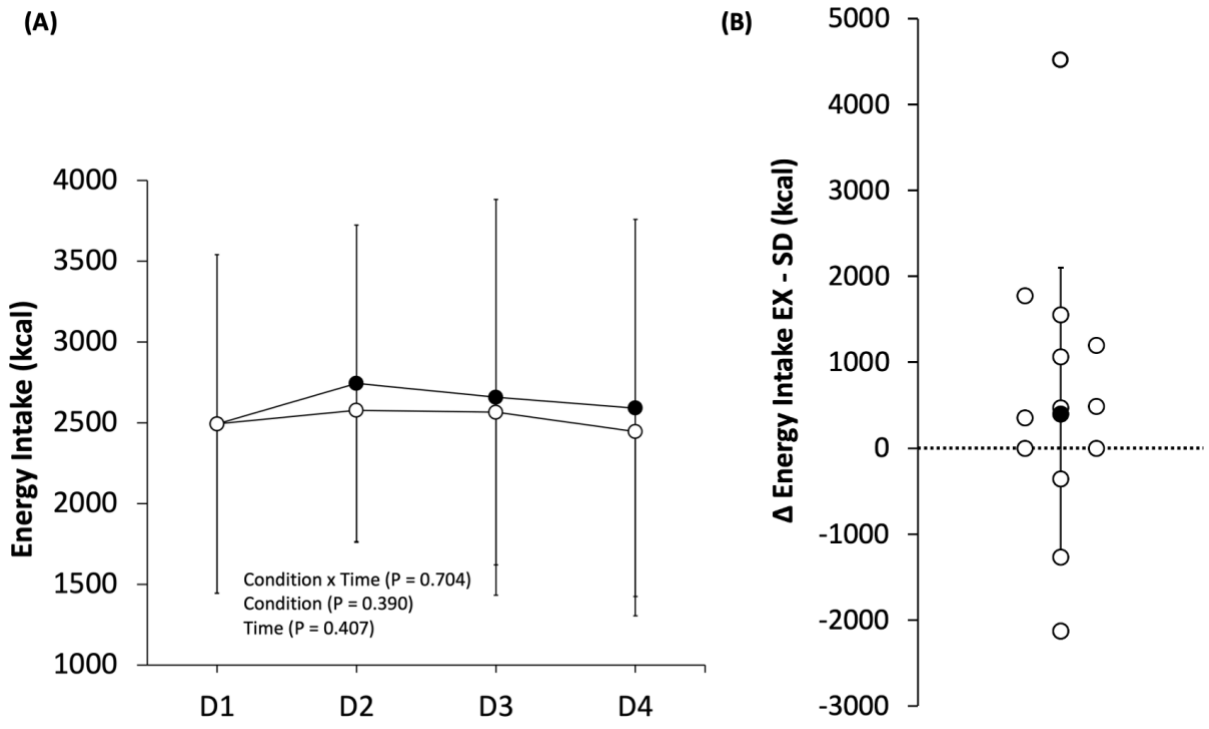

Figure 4.4 **Daily and individual measures of energy intake**
(A) Daily and **(B)** individual change in energy intake (EX condition – SD condition) over 4 days. For daily energy intake, open circles display the SD condition, while filled circles display the EX condition. For individual change in energy intake, open circles indicates each participant's change in energy intake, while the closed circle indicates the average change in energy intake between conditions. Values are means ± SD, n=14. SED, sedentary; EX, exercise.

4.5 Energy Expenditure and Sedentary Behaviour

A significant condition x time interaction (P < 0.001; η^2 = 0.58), main effect of condition (P = 0.003; η^2 = 0.51), and main effect of time (P < 0.001; η^2 = 0.62) was observed for energy expenditure between the exercise and sedentary conditions (Figure 4.5). Participants expended more energy on day 2 (P < 0.001; d = 1.74), as well as total energy expenditure (P = 0.003; d =

0.99) during the exercise condition compared to sedentary. No differences in energy expenditure were observed on day 1 (P = 0.065; d = 0.54), day 3 (P = 0.407; d = 0.23), and day 4 (P = 0.583; d = 0.15) between conditions.

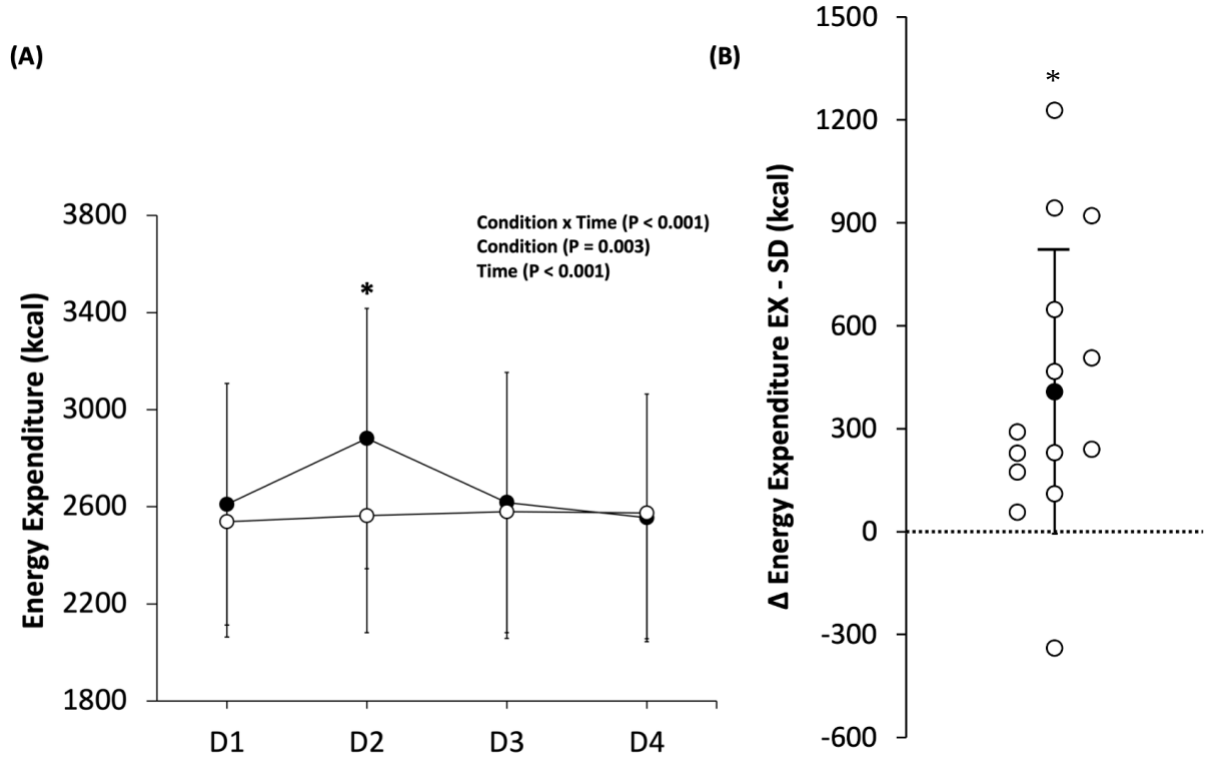

Figure 4.5 **Daily and individual measures of energy expenditure**
(A) Daily and **(B)** individual changes in energy expenditure (EX condition – SD condition) over 4 days. For daily energy expenditure, open circles display the SD condition, while filled circles display the EX condition. For individual change in energy expenditure, open circles indicates each participant's change in energy intake, while the closed circle indicates the average change in energy intake between conditions. *P<0.05 between EX and SD conditions. Values are means ± SD, n=14. SED, sedentary; EX, exercise.

No significant condition x time interaction was seen for time spent standing (P = 0.127; η^2 = 0.90); however, an interaction effect was observed for time spent sitting (P = 0.026; η^2 = 0.0.21), lying (P = 0.047; η^2 = 0.18), and number of steps (P < 0.001; η^2 = 0.63) (Table 4.2). No main effect of condition was observed for time spend standing (P = 0.444; η^2 = 0.05), sitting (P = 0.063; η^2 = 0.24), or lying (P = 0.987; η^2 = 0.00), however more steps were taken during the

Table 4.2 ActivPAL events

Day	Condition	Event (mean ± SD (range))			
		Time spent standing (hrs)	Time spent sitting (hrs)	Time spent lying (hrs)	Number of steps (x10^3)
D1	EX	3.6 ± 2.5 (0.6 - 8.3)	7.9 ± 2.6 (4.3 - 11.3)	9.8 ± 1.8 (5.9 - 13.8)	8.4 ± 5.6 (0.6 - 21.1)
	SED	2.7 ± (0.3 - 8.0)	8.2 ± 1.9 (5.0 - 12.0)	10.6 ± 2.6 (5.9 - 14.2)	6.3 ± 4.2 (0.3 - 13.8)
D2	EX	2.6 ± 2.0 (1.0 - 7.2)	7.6 ± 2.1 (4.4 - 11.5)*	9.9 ± 1.3 (7.6 - 11.4)	17.8 ± 4.0 (12.6 - 26.5)**
	SED	2.5 ± 2.0 (0.5 - 8.0)	9.9 ± 2.0 (4.9 - 12.3)*	9.0 ± 1.2 (7.6 - 11.6)	7.1 ± 4.9 (1.2 - 16.6)**
D3	EX	3.1 ± 1.8 (1.4 - 6.8)	8.1 ± 2.8 (3.4 - 13.1)	9.8 ± 1.3 (4.3 - 10.3)	8.4 ± 4.9 (1.5 - 17.9)
	SED	2.7 ± 2.1 (0.7 - 9.1)	9.9 ± 2.1 (5.1 - 13.7)	9.4 ± 1.4 (6.7 - 12.6)	7.3 ± 4.0 (2.0 - 14.6)
D4	EX	2.7 ± 1.2 (0.7 - 5.4)	9.9 ± 2.3 (5.8 - 13.1)	7.8 ± 1.5 (4.3 - 10.3)	6.5 ± 3.1 (1.8 - 12.3)
	SED	3.0 ± 1.9 (1.0 - 7.0)	9.6 ± 2.9 (5.1 - 13.3)	8.2 ± 1.5 (5.2 - 11.1)	7.3 ± 4.6 (2.0 - 18.5)
Total	EX	12.0 ± 6.6 (4.6 - 25.2)	33.4 ± 7.2 (19.8 - 46.1)	37.3 ± 3.8 (30.9 - 42.4)	41.1 ± 13.9 (22.8 - 70.6)*
	SED	10.8 ± 7.4 (2.5 - 30.6)	37.7 ± 7.5 (23.8 - 19.8)	37.2 ± 4.6 (29.9 - 46.6)	28.1 ± 16.6 (5.5 - 63.6)*

*$P < 0.05$ between exercise and sedentary conditions. **$P < 0.001$.

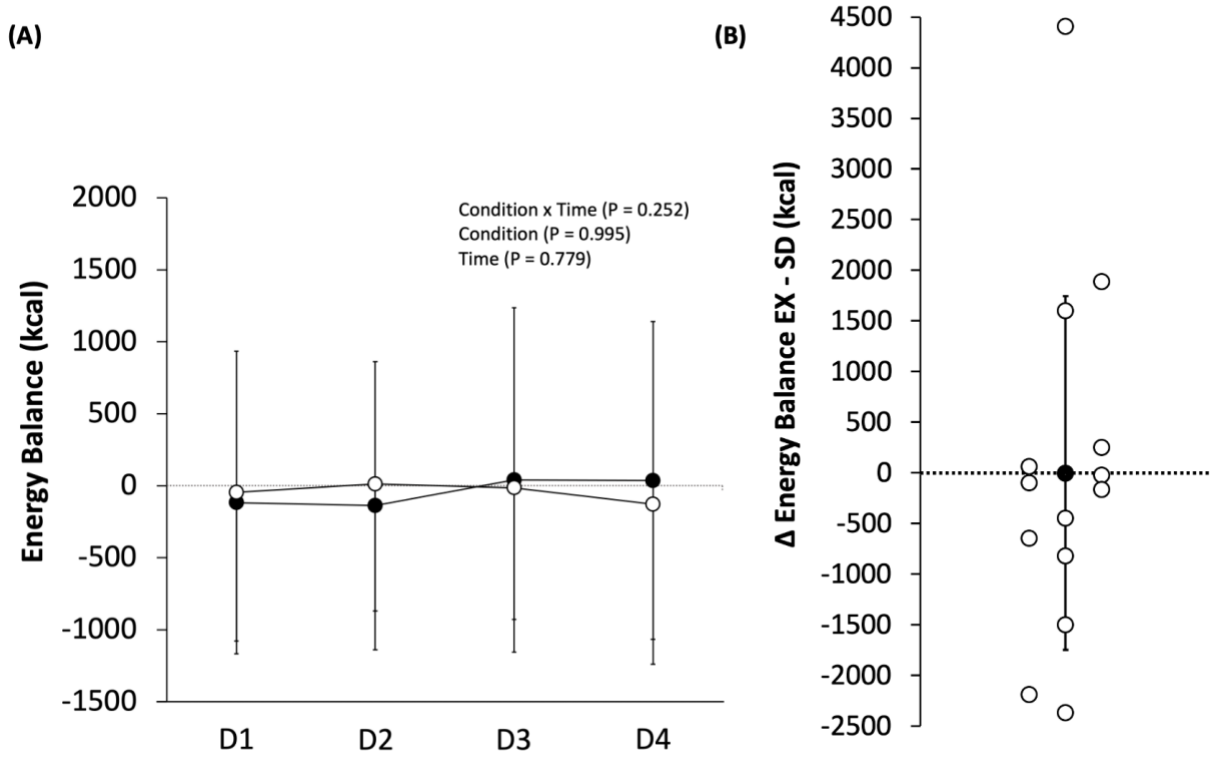

Figure 4.6 **Daily and individual measures of energy balance**
(A) Daily and **(B)** individual changes in energy balance (EX condition – SD condition) over 4 days. For daily energy balance, open circles display the SD condition, while filled circles display the EX condition. For individual change in energy balance, open circles indicates each participant's change in energy intake, while the closed circle indicates the average change in energy intake between conditions. Values are means ± SD, n=14. SED, sedentary; EX, exercise.

exercise trial ($P = 0.001$; $\eta^2 = 0.60$). A main effect of time was seen for sitting ($P = 0.007$; $\eta^2 = 0.26$), lying ($P < 0.001$; $\eta^2 = 0.39$), and steps ($P < 0.001$; $\eta^2 = 0.69$), but not standing ($P = 0.127$; $\eta^2 = 0.14$). Post-hoc analysis revealed significantly more time spent sitting on day 2 of the sedentary condition ($P = 0.007$; $d = 0.86$), but not for day 1 ($P = 0.515$; $d = 0.18$) or day 4 ($P = 0.774$; $d = 0.08$). There was a trend for more time seated on day 3 ($P = 0.054$; $d = 0.57$) and total time seated ($P = 0.063$; $d = 0.54$) during the sedentary condition compared to exercise. No differences in time spent lying were observed between conditions (Day 1: $P = 0.204$, $d = 0.36$;

Day 2: $P = 0.065$, $d = 0.54$; Day 3: $P = 0.302$, $d = 0.29$; Day 4: $P = 0.392$, $d = 0.24$; Total: $P = 0.987$, $d = 0.00$). Participants had higher step counts on day 2 ($P < 0.001$, $d = 1.86$) and total steps ($P = 0.001$, $d = 1.18$) during the exercise condition, but not on day 1 ($P = 0.056$, $d = 0.56$), day 3 ($P = 0.376$, $d = 0.24$), or day 4 ($P = 0.417$, $d = 0.22$).

4.6 Energy Balance

No condition x time interaction ($P = 0.252$), main effect of condition ($P = 0.995$), or main effect of time ($P = 0.779$) was observed for energy balance (energy balance = total energy intake – total energy expenditure) between the exercise and sedentary conditions (Figure 4.6). Daily (Day 1: $P = 0.065$, $d = 0.54$; Day 2: $P = 0.427$, $d = 0.22$; Day 3: $P = 0.779$, $d = 0.08$; Day 4: $P = 0.302$, $d = 0.29$) and total ($P = 0.995$; $d = 0.00$) energy balance was the same between conditions.

CHAPTER 5: DISCUSSION

Utilizing exercise independently as a weight loss strategy is a common, yet typically ineffective method to lower body weight (28, 29, 33). Although the underlying mechanisms that lead to less than anticipated weight loss with exercise is a topic of controversy, researchers have proposed that energy compensation through increased energy intake and/or reduced energy expenditure may be a contributor (37, 48, 160-162). To our knowledge, this is the first study to assess post-exercise appetite, energy intake, and energy expenditure over a 3-day post-exercise period using a standardized MRB. The aim of this study was to determine the prolonged, 3-day impact of a bout of aerobic exercise on energy compensatory mechanisms.

The main outcome measure was to accurately assess energy intake, while the secondary outcomes were perceived appetite, appetite-related hormones, and estimates of energy expenditure. Acutely, results from our study indicated lower fasted plasma concentrations of acyl-ghrelin between- and within- conditions immediately and 60 min post-exercise. No prolonged post-exercise impact was observed for appetite-related hormones, subjective appetite, or measures of energy compensation. However, our study indicated that participants felt less full and had a higher desire to eat over the 4-days during the exercise condition. This was further supported by a lower mean appetite score from the CSS, indicating lower levels of perceived satiety during the exercise condition. Finally, as expected, data from the activPAL4™ activity tracking devices demonstrated overall higher energy expenditure on day 2, as well as total energy expended over the 4-day exercise condition compared to the sedentary condition.

5.1 Acute Impact of Exercise on Appetite

5.1.1 Hormones Related to Appetite-Regulation

Studies investigating the acute effects of exercise on appetite and energy intake generally collect blood samples throughout various time points to examine objective measures of appetite-related hormones following a bout of exercise. In the present study, we obtained fasted blood samples at 3 time points on day 2, when participants completed the exercise or sedentary condition (baseline, immediately post-exercise/sedentary, 60 min post-exercise/sedentary) to measure fasted concentrations of plasma acyl-ghrelin, GLP-1, and total PYY. Our study demonstrated that fasted plasma concentrations of acyl-ghrelin were suppressed immediately and 60 min post-exercise when compared to the sedentary condition. Additionally, our results indicated that fasted plasma concentrations of acyl-ghrelin were suppressed immediately, and 60 min post-exercise relative to baseline measures within the exercise condition. These findings demonstrated that a 75 min bout of aerobic exercise at a high intensity (75% VO_{2peak}) transiently suppressed fasted plasma acyl-ghrelin and is reinforced by the large effect size that was observed. Additionally, our results are supported by previous studies examining the impact of exercise on appetite-related hormones (51, 52, 95, 163, 164). Broom et al. (51) completed a randomized crossover trial in a healthy male population comparing the effects of a 60 min bout of running on a treadmill at 70% of VO_{2max} compared to a sedentary condition. Results from the study indicated that concentrations of plasma acyl-ghrelin were lower over the first 3-hr and full 9-hr of the exercise trial when compared to the sedentary condition. Specifically, lower concentrations of plasma acyl-ghrelin were observed 30 min following the initiation of exercise and immediately post-exercise compared to the control. These findings are similar in comparison to our present study with a similar design of a randomized crossover trial and exercise intensity

(70% VO_{2max} vs 75% VO_{2peak}), where results demonstrated acute suppression of plasma acyl-ghrelin concentrations post-exercise, as well as overall lower plasma acyl-ghrelin concentrations during the exercise condition, compared to a sedentary control.

Although the general consensus among research literature is that exercise suppresses plasma acyl-ghrelin concentrations during exercise and transiently post-exercise (51, 52, 95, 102, 163, 164), research has also demonstrated no changes in post-exercise levels of acyl-ghrelin (122, 124). Hagobian et al. (124) investigated the effects of exercise on appetite hormones and energy intake in males and females. Participants completed exercise on a cycle ergometer at 70% VO_{2peak} until 30% of total daily energy expenditure was expended as well as 60 min resting control session in a crossover trial. Results from the study indicated no differences in plasma acyl-ghrelin immediately, 15 min, and 30 min post-exercise compared to the sedentary condition. Similar results were found in a study conducted by King et al. (122), where a 60 min brisk walk (~7 $km \cdot h^{-1}$) led to no differences in plasma concentrations of acyl-ghrelin during or post-exercise when compared to a sedentary control.

It has been suggested that performing exercise at a higher intensity may suppress acyl-ghrelin more consistently (51, 52, 95, 163, 164). This may explain the results observed by King et al., (102, 165) where a 60 min brisk walk led to no change in acyl-ghrelin post-exercise, whereas our results, as well as other studies with a similar exercise intensity (51, 52, 95, 163, 164), demonstrated an acute suppression of acyl-ghrelin during and/or post-exercise. However, this does not explain the findings from Hagobian et al. (124), where no changes in plasma acyl-ghrelin were observed following ~83 min of exercise at 70% VO_{2peak}. Additionally, Larson-Meyer and colleagues (166) demonstrated no differences in post-exercise concentrations of acyl-ghrelin between running or walking at 70% VO_{2max} (exercise-induced energy expenditure =

483.1 kcal·h^{-1} vs 305.1 kcal·h^{-1}, respectively) and sedentary control in females that were endurance trained and habitual walkers. Overall, these mixed findings suggest that exercise intensity and duration may play a role in post-exercise regulation of the orexigenic hunger hormone, acyl-ghrelin, where higher intensities and durations of exercise may more consistently suppress acyl-ghrelin (102, 105).

In addition to the hunger hormone acyl-ghrelin, a bout of aerobic exercise has been demonstrated to acutely impact plasma concentrations of satiety hormones GLP-1 and PYY. Our research demonstrated no changes in GLP-1 or PYY in healthy males and females following 75 min of running on a treadmill at 75% VO_{2peak} compared to a 75 min sedentary control. However, it is important to note that a large effect size was observed for PYY between conditions. Previous literature generally demonstrates acute increases in satiety hormones GLP-1 and PYY following a bout of aerobic exercise (91-94, 96, 102, 165), although studies have also found no changes in post-exercise GLP-1 and PYY (101, 123, 167, 168). Douglas et al., (93) found higher levels of GLP-1 and PYY in lean and overweight/obese male and female participants following a 60 min aerobic session on a treadmill at 59% VO_{2peak} compared to a sedentary control condition. In contrast, Beaulieu and colleagues (168) found mixed findings, with no change in GLP-1, but increased PYY in physically active males following 20 min of sprint interval exercise (4x 30 sec all out sprints with 4 min recovery). On the other hand, Balaguera-Cortes et al., (101) found no changes in post-exercise plasma PYY concentrations in active males following 45 min of running on a treadmill at 70% VO_{2peak} compared to a sedentary control.

The discrepancies in varying concentrations of GLP-1 and PYY post-exercise when comparing to a sedentary control trial has been speculated to be attributed to a multitude of factors including exercise intensity, sex of participants, and the time and state (fasted vs. fed) that

blood samples were collected (101, 105). A review by Hazell et al. (105) investigated the effect of exercise intensity and potential mechanisms that impact plasma concentrations of appetite-regulating hormones. Aerobic exercise performed at a moderate intensity (50-75% VO_{2max}) for 30-60 min was found to increase GLP-1 plasma concentrations, ranging from 16-1477% when compared to a non-exercise control condition. The lowest change in concentrations of GLP-1 were demonstrated by Martins and colleagues (91) in 12 healthy male and female participants following ~60 min of intermittent cycling (3x 17 min cycling with 3 min breaks) on a cycle ergometer at 65% of estimated maximal heart rate when compared to a resting condition. In contrast, the highest change in GLP-1 concentrations were observed in endurance trained females following a 60 min run at 70% VO_{2max} compared to 60 min of rest (166). For total PYY, Hazell and colleagues (105) found 30-90 min of moderate-intensity exercise (60-75% VO_{2max}) acutely increased total PYY by 8-172%. Similar to the findings for GLP-1, Martins and colleagues observed (91) the smallest change in total PYY concentrations following a bout of intermittent cycling. Beaulieu et al. (168) observed the highest increase in GLP-1 when compared to pre-exercise plasma concentrations.

Taken together, the lower, albeit significant increases in GLP-1 and PYY observed post-exercise had lower exercise intensities when compared to the highest changes observed for GLP-1 and PYY. However, this data does not coincide with the results from our study, where we observed no differences in fasted, post-exercise plasma levels of GLP-1 and total PYY despite having a generally higher intensity exercise protocol (75 min of running on a treadmill at 75% VO_{2peak}) compared to previous literature (91, 166, 168). It is important to note that the aforementioned studies provided a standardized breakfast for their participants prior to exercise (91, 166, 168), whereas participants from our study completed exercise and all blood draws in a

fasted state. This may in part explain why our results demonstrated no changes in post-exercise concentrations of fasted GLP-1 and PYY, as research has demonstrated lower levels of GLP-1 and PYY in a fasted state (58, 169), and conversely, increased levels of GLP-1 and PYY in the post-prandial state (64-66). This may suggest that the suppressed levels of GLP-1 and PYY associated with a fasted state may negate the anorexigenic impact of exercise on elevating GLP-1 and PYY.

In addition to variable responses of different exercise intensities and being in a fed vs. fasted state, sex may also acutely influence post-exercise appetite-related hormones. Studies investigating the acute impact of exercise on appetite-related hormones in a female population are limited (94, 166), as study design must control for potential fluctuations in appetite that are associated with the menstrual cycle (149-151). As the majority of studies investigating the impact of exercise on appetite and energy compensatory mechanisms mainly do so in male populations (101, 102, 168), our study aimed to include both male and female participants, as it is important to understand the influence of exercise on appetite regulation in both sexes.

Although we included both male and female participants, the primary aim of our study was not to measure sex differences in post-exercise appetite regulation. Analysis of appetite-related hormones based on sex demonstrated no differences for each trial. However, exercise has been demonstrated to influence appetite-related hormone response differently in males compared to females (94). Hazell et al. (94) investigated the impact of moderate-intensity continuous and sprint interval cycling exercise on sex differences in response to total PYY and GLP-1. GLP-1 was found to increase immediately post-exercise in both moderate-intensity continuous and sprint interval exercise in females, however this increase was not observed in males. Additionally, males were found to have a larger increase in PYY immediately post-exercise but

were also found to have larger decreases at 90 min post-exercise compared to females. These results demonstrate different sex responses over a 90 min post-exercise period at various exercise intensities for total PYY and GLP-1. Our study included both male and female participants, however, was not adequately powered to measure any potential sex differences. More research is needed to examine male vs. female differences in appetite-related hormone in response to exercise.

Overall, our current study and various other research has demonstrated no acute changes in total plasma concentrations of GLP-1 and PYY post-exercise. Although previous literature and review articles have consistently demonstrated acute elevations of GLP-1, and PYY post-exercise resulting in short-term exercise-induced anorexia. Discrepancies between our study and research that demonstrates acute exercise-induced anorexia may be attributed to different intensities of exercise and the impact of completing an exercise session in a fed vs. fasted state.

5.1.2 Acute Energy Compensation

A bout of exercise has been demonstrated to elicit acute anorexigenic effects, however, studies have reported mixed findings where an increase (126, 127), decrease (91), or no change (91, 101, 102, 122, 164) in energy intake was observed on the same day of exercise. The results from our study found that participants who performed 75 min of running on a treadmill at 75% VO_{2peak} did not increase absolute energy intake on the same day of exercise, when compared to a 75 min sedentary control condition. Similar findings were observed by Vatansever-Ozen et al. (125) where a prolonged, 120 min bout of exercise at ~50% maximal oxygen uptake did not stimulate increases in absolute energy intake when compared to a control condition. Hagobian and colleagues (124) also demonstrated no changes in absolute measures of energy intake following a standardized exercise protocol to expend 30% of total daily energy expenditure. Additionally,

research with similar study design and exercise intensity found no changes to energy intake on the same day of exercise (53). These studies provided *ad libitum* buffet style meals within a laboratory setting throughout the day and measured energy intake by weighing leftovers from the meals. Assessment of *ad libitum* energy intake through buffet style meals has been demonstrated to be reproducible (121). However, consuming meals in an unfamiliar environment with time constraints, and standardized timing of meals may potentially influence *ad libitum* energy intake.

To address this concern, our study utilized a take-home MRB diet so that participants could consume meals *ad libitum* in a free-living condition, though the use of a liquid MRB diet has yet to be utilized to measure post-exercise energy intake. Previous literature that has utilized liquid diets have been implemented as a diet for individuals with morbid obesity prior to bariatric surgery and have demonstrated high levels of adherence to the diet (170-172). Longer durations (7-14 days) on an exclusive liquid diet have previously been shown to lead to less compliance and adherence (170), suggesting that our 4-day liquid MRB was tolerable, especially with the initial test trial.

Besides providing *ad libitum* meals within a laboratory setting to participants, another potential inaccuracy in determining energy intake may be due to the method of measuring food intake. Jokisch et al. (126) conducted a study where energy intake was recorded 60 min post-exercise in the form of an *ad libitum* buffet within a laboratory setting and found lower caloric intake following exercise compared to a control condition in inactive males. Conversely, the same study by Jokisch and colleagues (126) demonstrated overall higher energy intake following the exercise trial for the remainder of the day following each exercise or control protocol. Importantly, the measures of energy intake outside of the laboratory were reported using a self-reported food record. A study by Poslusna, et al. (53) investigated misreporting of energy intake

by food records and 24 hr recalls and found that 30% of participants under-reported energy intake by approximately 15%. Additionally, as previously mentioned, an *ad libitum* buffet consumed within a laboratory setting may impact energy intake due to an unfamiliar environment, time constraints, and standardized timing of meals.

Another potential factor that may have impacted measures of post-exercise energy intake was whether participants were active vs. inactive. Our study took baseline measures of physical activity using a self-reported questionnaire (145), although no exclusion criteria for participants were based on this data. The amount of self-reported physical activity ranged from 3 – 89 $MET \cdot h \cdot wk^{-1}$, indicating that our sample included both active and inactive individuals. Jokisch et al. (126) demonstrated active males who regularly exercise may acutely compensate to an exercise-induced energy deficit through increased energy intake on the same day of exercise. Whereas inactive males who do not exercise on a regular basis may not respond to an exercise-induced negative energy balance through increases in energy intake in the subsequent meal following a bout of exercise (126). Due to the inclusion of both active and inactive participants in our study, measures of energy intake on the same day that exercise was performed may have been impacted. Altogether, inconsistencies in acute measures of energy intake on the same day of exercise may be influenced by the training status of participants, as well as the methods in which energy is measured.

As expected, overall energy expenditure was higher during the day of exercise when compared to the sedentary condition. No differences in time spent standing, sitting, or lying were observed on the same day of exercise. Previous literature has demonstrated decreases in energy expenditure on the same day of exercise (173), although increases (174) and no changes (175-177) in post-exercise energy expenditure have also been demonstrated. Kriemler et al. (173)

observed reduced energy expenditure and spontaneous bouts of physical activity on the same day that moderate or strenuous exercise was performed compared to a control condition in adolescent males with obesity. The contrasting findings from our study may be due to differences in participant demographics (healthy young male and female adults vs. adolescent males with obesity) and exercise intensity (75 min at 75% VO_{2peak} vs. 4x 10 min cycling with 5 min rest at HR 150-160 bpm) (173). Conversely, Wang & Nicklas (174) demonstrated overall lower levels of energy expenditure on the same day a bout of vigorous exercise was performed compared to a non-exercise control, whereas moderate exercise did not induce the same effect in postmenopausal women. This is interesting, as higher levels of energy expenditure are expected to be produced on the day that exercise was performed compared to a non-exercise control. These results indicate that postmenopausal women may expend more energy through non-structured physical on days that have no prescribed exercise, compared to a day with prescribed vigorous exercise. Another interpretation from the findings is that NEAT was reduced following a bout of vigorous exercise. However, these results cannot be generalized as they were demonstrated in postmenopausal females with overweight or obesity who previously underwent 5 months of caloric restriction prior to the exercise session (174).

The discrepancies in previous literature compared to our study for same day post-exercise energy expenditure may be due to varying measures of energy expenditure. Our current study, as well as Kriemler and colleagues (173) measured estimated levels of energy expenditure using an activity tracking device, whereas, Cadieux et al. (175) recorded energy expenditure using a portable indirect calorimetry unit. Though a different method was used to measure energy expenditure, Cadieux et al. (175) demonstrated similar findings to our current study, where no differences in post-exercise total energy expenditure and NEAT in normal weight males and

females was observed (175). Similar to literature regarding the acute impact of exercise on energy intake, there are mixed findings in various populations, demonstrating an increase, decrease, or no change in energy expenditure and NEAT on the same day that exercise was performed. Contrasting findings from our study compared to previous literature may be due to differences in exercise intensity and the method of determining energy expenditure following a bout of exercise.

5.1.3 Subjective Appetite

Similar to the changes that occur to hormones related to appetite regulation, a bout of exercise has been demonstrated to impact levels of subjective appetite (51, 52, 164). The results from our study demonstrated no acute differences in subjective ratings of appetite following a bout of exercise. These results conflict with literature investigating the acute impact of exercise on levels of subjective appetite, where exercise-induced anorexia is generally observed (102). However, studies have also observed no acute post-exercise changes in subjective feelings of appetite (51, 52, 91, 102, 163).

A review by Dorling et al., (102) found that a bout of exercise performed at an intensity greater than 60% VO_{2peak} typically led to exercise-induced anorexia. The exercise-induced anorexia is a result of an acute decrease in subjective appetite and is supported by the changes observed when measuring post-exercise appetite-related hormones, where a decrease in the hunger hormone acyl-ghrelin and increase in satiety hormones GLP-1 and PYY are generally observed (102). A study by King et al. (52) demonstrated suppressed levels of perceived hunger and PFC at 0.5, 1, and 1.5 hr during and immediately after the 90 min exercise condition compared to a sedentary control. Higher levels of subjective fullness and satisfaction were observed at 0.5 and 1 hr during the exercise condition. These results demonstrate that hunger and

PFC are suppressed, whereas feelings of fullness and satisfaction are increased during and immediately after exercise (52). Conversely, Martins et al. (168) demonstrated no suppression of hunger acutely after exercise in individuals with overweight or obesity.

One potential variable that may have influenced the findings from our study is the timing at which measures of subjective appetite were measured. Our study only measured levels of subjective appetite immediately, 60 min post-exercise, ~1700 hr, and before bed on the same day that exercise or sedentary sessions were performed. Other studies took perceived measures of appetite during exercise, which typically leads to suppression of perceived appetite, as well as appetite-related hormones (52, 168). Similar to the variable findings on post-exercise regulation of appetite-related hormones, exercise intensity, duration, and fed vs. fasted state may also impact perceptions of hunger during and post-exercise. A brisk walk was demonstrated to have no influence on perceived appetite (178), whereas a 90 min moderate intensity run transiently suppressed appetite during and immediately after exercise (178). Additionally, fed participants demonstrated suppressed levels of hunger during an exercise session (51, 52, 95, 163, 164), whereas our study demonstrated no acute differences in subjective appetite in a fasted state following exercise. Although our acute findings for post-exercise concentrations of satiety hormones and subjective appetite are supported by previous literature, inconsistencies with contrasting studies may be related to exercise intensity, duration, timing of measures, and whether participants exercised in a fed or fasted state.

5.2 Prolonged Impact of Exercise on Appetite

5.2.1 Hormones Related to Appetite-Regulation

The impact of exercise on measures of subjective appetite and appetite-related hormones have been well documented on the same day of exercise, however less research has investigated the

prolonged impact of exercise on appetite, beyond the 24 hr post-exercise period (178). Although previous literature typically suggests that exercise acutely suppresses appetite (178), studies have demonstrated less than anticipated levels of weight loss with exercise (28, 33-36). Changes in subjective appetite and appetite-related hormones that lead to increased energy intake have been suggested to play a role in energy compensation with exercise (102, 165). Therefore, it is important to understand the prolonged impact exercise has on physiological regulators of appetite.

Our study aimed to measure objective markers of appetite and levels of perceived appetite over a 3-day post-exercise period. The results from our study indicated no prolonged impact of aerobic exercise on appetite markers of acyl-ghrelin, PYY, or GLP-1 relative to a control session. Research investigating the 2-day impact of exercise on appetite has demonstrated similar and contrasting findings to our study (168, 178). A randomized crossover study examining the effects of exercise on appetite and energy intake over a 2-day period demonstrated no changes in plasma acyl-ghrelin concentrations between the exercise and sedentary control conditions, although higher overall levels of PYY were observed during the exercise condition (178). The sample consisted of 15 healthy males, where participants completed a bout of exercise at 70% VO_{2peak} for 60 min running on a treadmill, during the morning of day 1 and day 2 for the exercise condition and 60 min sedentary session during the control condition. A total of 7 venous blood samples were collected throughout the study to assess hormones related to appetite-regulation (day 1: 0, 7 h; day 2: 0, 2, 3, 6, and 7 h). Although the research conducted by Douglas et al., is comparable to the current study in methodology and exercise protocol, there are some notable differences. The blood draws completed by Douglas et al., (178) did not include measures during or immediately after exercise, whereas the current study collected blood samples during and/or

immediately after exercise. Additionally, Douglas and colleagues (178) designed their study so that participants completed a bout of exercise each morning over the 2-day trial. This may explain why overall concentrations of PYY were higher during exercise, as PYY is typically elevated following a bout of exercise (91, 166), whereas our study demonstrated no 3-day differences in PYY following a single bout of aerobic exercise. Additionally, two blood draws were taken 1-hr following an *ad libitum* meal (178), which may have influenced the overall increase in PYY, as PYY has been demonstrated to rise in the post-prandial state (66-68). All blood draws for our study were completed in a fasted state of >10 hrs. Concentrations of PYY are generally low and progressively decline in the fasted state, whereas transient increases in circulating PYY are observed in the post-prandial state (68, 169). The regulation of PYY in the fed vs. fasted state may explain why we did not observe any differences in PYY between the exercise and sedentary conditions over a 3-day period.

Overall, our study observed no 3-day post-exercise changes to fasted concentrations of acyl-ghrelin, GLP-1, and PYY. Collecting additional blood samples throughout each day, in both fasted and standardized, post-prandial states, may provide a better understanding of the prolonged impact of exercise on markers of appetite.

5.2.2 Prolonged Energy Intake

The results from our study indicated that exercise had no impact on energy compensation through increased energy intake over a 4-day period. These findings contrast our hypothesis that a bout of aerobic exercise would stimulate energy compensation through increased energy intake. Our original hypothesis was based on previous literature that has extensively reviewed the impact of chronic exercise interventions on energy compensatory mechanisms (30, 49, 102,

162), as well as speculations that previous research investigating post-exercise energy compensation may have inaccurate measures of energy intake. Researchers have postulated that the human body may partly compensate for the exercise-induced energy expenditure through potential increases in energy intake (30, 49, 102, 162). Our study design and primary measure was to investigate levels of energy intake following a single bout of aerobic exercise over a total of 4-days. Our study utilized a novel MRB diet to accurately measure energy intake in a free-living situation as misreporting of energy intake by food records and 24 hr recalls have been demonstrated to be inaccurate (53). Further, studies that do not utilize food journals and 24 hr recalls generally measured energy intake by weighing leftover foods from *an ad libit*um buffet style meal. This may potentially impact energy intake due to the unfamiliar laboratory environment, time restraints (typically ~30 min) to finish a meal, as well as standardized timing of the meals.

The findings from our study were supported by previous research with similar multi-day crossover designs, where no increase in energy expenditure was observed over a 2-day post-exercise period (168, 178). Beaulieu et al. (168) demonstrated no differences in total energy intake following 2 days of exercise compared to a sedentary control condition. Similarly, Douglas and colleagues (178) demonstrated no changes to total energy intake over a 2-day period comparing exercise and sedentary conditions. Prolonged studies that investigate post-exercise energy compensation beyond the 24–72-hour post-exercise period begin to demonstrate partial compensation through increased energy intake. A study by Stubbs et al. that investigated the impact of moderate- and high-intensity exercise compared to a sedentary control on energy intake and balance and was separated into male (179) and female (180) results. The results demonstrated no compensatory energy intake in males, however partial compensations in energy

intake were observed in females during the exercise conditions over a 7-day period. These findings suggest that females may begin to compensate for exercise-induced energy expenditure as early as 7-days during moderate- and high-intensity exercise (180). On the other hand, males were found to have no change in energy intake over the 7-day trials and were in a substantially negative state of negative energy balance (179). The authors findings suggest that males may be able to tolerate a large state of exercise-induced negative energy balance without inducing a compensatory increase in energy intake over a 7-day period (179). However, the results demonstrated by Stubbs and colleagues (179, 180) should be evaluated with care, as there are several limitations with the study. Firstly, measures of energy expenditure were estimated by continual heart rate monitoring, which may have led to inaccurate measures of energy expenditure, compared to more accurate measures, such as indirect calorimetry using a metabolic cart (181) and a metabolic chamber (182). Additionally, measures of energy intake were recorded using a self-reported food diary which have been demonstrated to underreport food intake (53).

As our current study did not show any compensatory increases in energy intake over a 4-day period, there is a possibility that a longer duration study that encompasses >7 days post-exercise may induce compensatory increases in energy intake due to exercise-induced energy expenditure. A review by Riou et al. (162) observed lower levels of energy compensation during shorter-term exercise interventions (< 25 wks), although the studies analyzed were highly variable in the degree of energy compensation. The variance in energy compensation was associated with an interaction with the duration of exercise-interventions, as well as initial fat mass, and age of the participants. Longer-term exercise interventions (> 80 wks) were found to have much higher levels of compensation through increased energy intake (162). Differences on

the impact of varying length of exercise protocols on energy compensation is demonstrated in a 10-week exercise study that demonstrated 17% energy compensation (183) compared to a 70-week intervention that demonstrated 100% energy compensation (184). The authors found that sex, frequency, intensity, and dose of exercise-induced energy expenditure did not predict level of energy compensation (162). We are unable to compare our findings with long-term exercise interventions, as duration of exercise protocol has been demonstrated to be associated with variance in energy compensation (162). Additionally, long-term exercise interventions involve multiple sessions of exercise per week, whereas our study investigated the impact of a single bout of aerobic exercise on energy intake over a 3-day post-exercise period. In addition to increased energy intake, studies have suggested that exercise leads to compensatory decreases in energy expenditure (162).

5.2.3 Prolonged Energy Expenditure

Previous literature investigating the chronic impact of exercise on energy compensation generally focuses on measures of energy intake rather than energy expenditure. However, reduced energy expenditure due to compensation of exercise-induced energy expenditure has been previously demonstrated (42, 179, 180). The results from our study demonstrated higher overall energy expenditure during the exercise condition compared to the sedentary condition. Specifically, higher energy was expended during day 2 when exercise was performed and is supported by the large effect sizes observed. Similar findings were demonstrated over a 7-day exercise intervention, where exercise interventions produced higher levels of energy expenditure compared to a control condition (179, 180). However, a trend was observed where total daily energy expenditure declined progressively over the 7-day exercise condition, compared to the

control suggesting decreased levels of NEAT (179, 180). The measures of energy expenditure were based on estimates through continuous heart rate monitoring and may have potentially influenced results from the studies. Although, a decline in NEAT over a 7-day period due to exercise is supported by a study by Riou and colleagues (42) investigating the effects of a 3-month exercise intervention in females with overweight or obesity. The results from the study demonstrated almost full energy compensation for exercise-induced energy expenditure through a compensatory decrease in non-structured physical activity within the first week of a 3-month exercise intervention and persisted throughout the remainder of the intervention. These findings suggest that our current study may have observed compensatory changes to non-structured physical activity due to exercise-induced energy expenditure if we extended our 4-day trial to 7 or more days.

Conversely, Myers et al. (139) demonstrated no compensatory changes to non-exercise physical activity following a 12-week exercise intervention in inactive females with overweight or obesity. These results support our findings where no decreases in energy expenditure were observed 3-day post exercise and similarly used an activity tracker to estimate energy expenditure as well as sedentary behaviour. However, it is important to note the differences in participant demographics, where our study recruited healthy young adult males and females, compared to the inactive female participants with overweight and obesity that were recruited by Myers and colleagues (185). Overall, studies investigating the prolonged and chronic impact of exercise on energy compensatory mechanisms demonstrate mixed findings and requires further research with more accurate measures of energy intake and energy expenditure.

5.2.3 Subjective Appetite

Interestingly, the results from our study demonstrated overall lower levels of perceived fullness and higher PFC over the 3-day post-exercise period compared to the sedentary condition. Further, when taking the mean appetite rating score using the CSS, we observed a decrease in the CSS during the exercise condition compared to the sedentary condition indicating lower levels of perceived satiety. Additionally, although no statistical significance was observed between conditions for levels of hunger and satisfaction, large effect sizes for hunger and satisfaction were observed between the exercise and sedentary conditions, where participants felt increased levels of hunger and decreased feelings of satisfaction during the exercise condition.

Our present findings of increased perceptions of appetite are supported by previous articles investigating the prolonged impact of exercise on appetite (31, 32, 168). Similar findings to our study were demonstrated by Beaulieu and colleagues (168), where overall ratings of hunger and PFC were higher over a 2-day post-exercise period when compared to a sedentary control condition. More recently, a review by Beaulieu et al. (186) demonstrated a small increase in fasting levels of perceived hunger during an exercise intervention with little to no increases in overall energy intake when compared to non-exercise control conditions in adults with overweight or obesity. These findings are supported by our current study where an overall increase in PFC combined with a decrease in feelings of fullness and CSS are demonstrated with no changes in overall energy intake over a 4-day period.

Although exercise is generally thought to elicit an increase in energy intake to compensate for the energy expended during exercise (162), our study and the recent review by Beaulieu et al. (186) do not demonstrate compensation due to increased energy intake, despite increased perceptions of appetite. This increase in subjective appetite following exercise with no

compensation may be due to exercise increasing dietary restraint and decreased disinhibition (186-189). King and colleagues (187) investigated the impact of a 12-week exercise intervention (2500 kcal·wk^{-1}) on levels of subjective appetite and satiating efficiency of a fixed meal in males with overweight or obesity. The findings from the study demonstrated an increase in fasted and total levels of perceived hunger compared to baseline following the 12 week exercise intervention. Conversely, an increase in the satiating effect of a fixed meal from the prescribed exercise was observed (187). The increased fasted levels of perceived hunger contrasts the increase in satiety from a fixed meal due to exercise. This has been suggested to be due to a dual effect of exercise, where an increase in the sensitivity of physiological appetite signalling leads to a higher satiating effect of a fixed meal, despite having higher levels of hunger at the end of the 12 week exercise intervention (187).

In addition to the increased satiety associated with exercise (187), it has been suggested that eating behaviour, as well as food reward/preferences may be impacted by exercise to reduce an individual's susceptibility to overconsumption (186). Studies have demonstrated that exercise interventions lead to improved eating behaviour through decreased uncontrolled eating (186, 190, 191) and improved food reward/preferences (186, 190-192). On the other hand, our study did not demonstrate overall increases in subjective hunger or satisfaction over a 4-day period, although a trend was observed, where exercise had higher levels of hunger and lower satisfaction. Douglas et al. (178) demonstrated no 2-day post-exercise change in levels of perceived hunger, satisfaction, fullness, or PFC. Despite many similarities to the study methodology that Douglas and colleagues utilized (178), we demonstrated increased levels of PFC and lower feelings of fullness during exercise, although our study also observed no changes to feelings of hunger or satisfaction. The discrepancies in our findings may be attributed to the

additional exercise session that was performed (178) compared to our single bout of exercise. However, consistently exercising has also been demonstrated to have no impact on ratings of perceived appetite (188, 193). The disagreement with perceived fullness, PFC, and CSS may in part be due to additional measures of subjective appetite collected at 5pm, and before bedtime on each of the 4 days for exercise and sedentary conditions. During these times, we were unable to standardize the nutrient intake for participants prior to subjective assessments of appetite. Taken altogether, exercise may increase perceived levels of appetite while simultaneously increasing post-prandial satiety scores and improving eating behaviour, which may in part account for no compensatory increases in energy intake observed with exercise.

5.3 Strengths and Limitations

This study design was a randomized, counterbalanced crossover trial, which allowed us to mitigate potential individual variation effects to assess the 3-day post-exercise appetite and energy compensatory mechanisms. A common weakness of a crossover design is participant dropout, where different dropout rates may occur between conditions. A generally acceptable dropout rate for crossover trials is 20%, although, inaccurate conclusions may still be made with dropout rates below 20% (194). Fortunately for our study, there were no participants that dropped out. This may be partly due to the test trial completed prior to recruitment of participants to assess their ability to tolerate a liquid MRB diet. Participants were also incentivized to continue the study through a monetary payment of $50 for each 4-day condition that was completed, totaling $100 for completing the study.

Due to the design of the study and the limited time we had to complete data collection, our sample size was relatively small (N = 14). Most studies investigating the impact of exercise on appetite and energy compensatory mechanisms mainly do so in male populations (101, 102,

168). This is due to controlling for potential appetite fluctuations associated with the menstrual cycle in females (149-151). It just as important to investigate post-exercise appetite and energy compensatory mechanisms in male and female populations, so our study aimed to be inclusive to both males (N = 8) and females (N = 6). However, it is important to note that our participants were young, healthy male and female volunteers, so our data is not generalizable to individuals with overweight/obesity, or young adolescent or older populations.

This is the first study to measure energy intake following a bout of exercise using an exclusive MRB diet over a 4-day period. However, liquid diets have been commonly utilized in different studies following individuals with morbid obesity prior to bariatric surgery and have been demonstrated to have high adherence and compliance (170-172). There are various strengths and weaknesses with this style of measuring energy intake. Firstly, participants must be able to tolerate and exclusively consume a liquid diet consecutively over a 4-day period. Consuming a liquid diet for 4 consecutive days does not represent a typical North American diet, and participants may be less motivated to consume the MRB even when their appetite is high. This is partly demonstrated by the results from subjective appetite ratings, where participants felt less full and had higher PFC during the exercise condition. In our study, participants were provided a daily excess amount of the MRB, that had nutritional labels removed to blind caloric intake, to consume *ad libitum*. Participants were required to bring back all full, partially full, and empty bottles of the MRB drinks, as well as the wrapper for the fibre bar to the lab each morning and verbally confirmed that they exclusively consumed the MRB drinks, fibre bar, and water. This style of take-home meals allows participants to enjoy a free-living setting, whereas other studies that provide *ad libitum* buffet style meals in the lab do so in a secluded room, and typically must be eaten within a given duration (e.g., 30 min) (93, 101, 164, 195). Food journals and recalls

have also been used as a way to assess daily energy intake; however, this method has been shown to have inaccuracies (53). An additional strength for our study is the standardization of energy intake on day 1, prior to the intervention day on day 2.

Another strength of our study is the inclusion of the activPAL4™ activity tracker to estimate daily energy expenditure and time spent standing, sitting, and lying and has been demonstrated to be a valid and reliable measure of posture and motion (196). However, there are multiple limitations to the activPAL4™ software. The activPAL4™ may not accurately discriminate between the sitting and lying postures due to the positioning of the device on an individual's thigh (197). Additionally, researchers that are unfamiliar with R software and coding are unable to categorize various intensities of exercise within the provided software.

Finally, a notable limitation for our study includes the collection of data during a global pandemic due to the coronavirus disease (COVID-19). A global questionnaire comparing eating behaviour and physical activity prior to and during COVID-19 restrictions was conducted by Ammar and colleagues (198). Results from the questionnaire demonstrated decreased levels of physical activity, as well as increased time spent sitting during the COVID-19 restrictions, compared to previously normal living conditions. Additionally, participants indicated more unhealthy dietary behaviours, such as an increased preference for unhealthy foods, binge eating, and snacking more often. The mandatory isolation restrictions implemented to decrease transmission of COVID-19 has also been demonstrated to impact mental health, where increases in levels of stress, anxiety, symptoms of depression, insomnia, anger, and fear were observed on a global scale (199). The challenges and overall negative health impact that COVID-19 restrictions have on an individual's lifestyle and mental health are likely to have impacted the results of our study, although the precise impact of the pandemic on our study is not known.

5.4 Summary and Future Directions

The worldwide problem of overweight and obesity presents a risk to health in individuals and burdens the health care system. With exercise being so heavily promoted as a method for weight loss, it is crucial that we understand the compensatory mechanisms that attenuate decreases in body weight. Overall, our study aimed to investigate the prolonged 3-day impact of a bout of aerobic exercise on measures of subjective appetite, appetite-related hormones, energy intake, and energy expenditure. This study had 3 main findings: firstly, a bout of aerobic exercise acutely suppressed fasted concentrations of acyl-ghrelin immediately and 1 hr post-exercise; secondly, exercise altered overall measures of perceived appetite, where participants felt less full, had a higher motivation to eat, and lower feelings associated with satiety over the 4-day exercise condition; and finally, higher energy was expended during the exercise trial for the overall 4-day period, where more energy was expended during day 2 on the same day of exercise. No changes in overall acyl-ghrelin, GLP-1, PYY, perceived hunger, satisfaction, or *ad libitum* energy intake were observed between exercise and sedentary conditions. These findings support previous literature that demonstrates acute post-exercise suppression of acyl-ghrelin with no changes to 3-day post-exercise compensatory increases in food intake (52) despite decreased perception of fullness, satiety, and increased PFC and energy expenditure during the exercise condition (168).

While ours was a shorter-term study, individuals utilizing exercise in an attempt to lose weight should do so with caution, as longer-term data has demonstrated higher levels of energy compensation (162). However, that is not to say that individuals should not participate in physical activity, as exercise has been demonstrated to promote health benefits independent of weight loss (200). Exercise, in the absence of weight loss, can improve cardiorespiratory fitness

and reduce resting HR, which are both associated with lower risk of CVD and all-cause mortality (201). Additionally, exercise has been demonstrated to improve body composition, contributing to higher fat-free mass relative to fat mass (200). This is important, as a reduction in fat-free mass, particularly skeletal muscle, can result in adverse metabolic effects. Exercising has also been demonstrated to increase self-perception of health and improve emotional well-being, regardless of weight-loss.

This is the first study to measure the 3-day post-exercise energy intake response using a standardized liquid MRB. Future studies should investigate an extended 7-day post-exercise period to induce compensatory responses and explore more precise measures of energy expenditure such as a metabolic chamber (182). Our study demonstrated that a test trial to test a participant's ability to tolerate a liquid diet resulted in no participants dropping out of the main intervention conditions. Future studies utilizing a standardized MRB to measure energy intake should continue to implement a test trial to limit potential dropout. Taken altogether, individuals that are planning on losing weight with exercise should be wary of potential energy compensatory increases in energy intake and decreases to non-structured physical activity over the long term. Health professionals should increase awareness about potential energy compensation that is associated with exercise and that health benefits, independent of weight, should be the primary focus of exercise.

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APPENDIX A: GET ACTIVE QUESTIONNAIRE (GAQ)

CSEP | SCPE
THE GOLD STANDARD IN EXERCISE SCIENCE AND PERSONAL TRAINING

Get Active Questionnaire

CANADIAN SOCIETY FOR EXERCISE PHYSIOLOGY –
PHYSICAL ACTIVITY TRAINING FOR HEALTH (CSEP-PATH®)

Physical activity improves your physical and mental health. Even small amounts of physical activity are good, and more is better.

For almost everyone, the benefits of physical activity far outweigh any risks. For some individuals, specific advice from a Qualified Exercise Professional (QEP – has post-secondary education in exercise sciences and an advanced certification in the area – see csep.ca/certifications) or health care provider is advisable. **This questionnaire is intended for all ages – to help move you along the path to becoming more physically active.**

☐ I am completing this questionnaire for myself.

☐ I am completing this questionnaire for my child/dependent as parent/guardian.

PREPARE TO BECOME MORE ACTIVE

The following questions will help to ensure that you have a safe physical activity experience. Please answer YES or NO to each question before you become more physically active. If you are unsure about any question, answer YES.

	YES	NO
1	Have you experienced **ANY** of the following (A to F) **within the past six months**?	
A	A diagnosis of/treatment for heart disease or stroke, or pain/discomfort/pressure in your chest during activities of daily living or during physical activity?	○ ○
B	A diagnosis of/treatment for high blood pressure (BP), or a resting BP of 160/90 mmHg or higher?	○ ○
C	Dizziness or lightheadedness during physical activity?	○ ○
D	Shortness of breath at rest?	○ ○
E	Loss of consciousness/fainting for any reason?	○ ○
F	Concussion?	○ ○
2	Do you currently have pain or swelling in any part of your body (such as from an injury, acute flare-up of arthritis, or back pain) that affects your ability to be physically active?	○ ○
3	Has a health care provider told you that you should avoid or modify certain types of physical activity?	○ ○
4	Do you have any other medical or physical condition (such as diabetes, cancer, osteoporosis, asthma, spinal cord injury) that may affect your ability to be physically active?	○ ○

NO to all questions: go to Page 2 – ASSESS YOUR CURRENT PHYSICAL ACTIVITY ➤

YES to any question: go to Reference Document – ADVICE ON WHAT TO DO IF YOU HAVE A YES RESPONSE ➤➤

Get Active Questionnaire

ASSESS YOUR CURRENT PHYSICAL ACTIVITY

Answer the following questions to assess how active you are now.

1 During a typical week, on how many days do you do moderate- to vigorous-intensity aerobic physical activity (such as brisk walking, cycling or jogging)? ____ DAYS/WEEK

2 On days that you do at least moderate-intensity aerobic physical activity (e.g., brisk walking), for how many minutes do you do this activity? ____ MINUTES/DAY

For adults, please multiply your average number of days/week by the average number of minutes/day: ____ MINUTES/WEEK

Canadian Physical Activity Guidelines recommend that adults accumulate at least 150 minutes of moderate- to vigorous-intensity physical activity per week. For children and youth, at least 60 minutes daily is recommended. Strengthening muscles and bones at least two times per week for adults, and three times per week for children and youth, is also recommended (see csep.ca/guidelines).

GENERAL ADVICE FOR BECOMING MORE ACTIVE

Increase your physical activity gradually so that you have a positive experience. Build physical activities that you enjoy into your day (e.g., take a walk with a friend, ride your bike to school or work) and reduce your sedentary behaviour (e.g., prolonged sitting).

If you want to do **vigorous-intensity physical activity** (i.e., physical activity at an intensity that makes it hard to carry on a conversation), and you do not meet minimum physical activity recommendations noted above, consult a Qualified Exercise Professional (QEP) beforehand. This can help ensure that your physical activity is safe and suitable for your circumstances.

Physical activity is also an important part of a healthy pregnancy.

Delay becoming more active if you are not feeling well because of a temporary illness.

DECLARATION

To the best of my knowledge, all of the information I have supplied on this questionnaire is correct.
If my health changes, I will complete this questionnaire again.

I answered NO to all questions on Page 1

Sign and date the Declaration below

I answered YES to any question on Page 1

Check the box below that applies to you:

- ☐ I have consulted a health care provider or Qualified Exercise Professional (QEP) who has recommended that I become more physically active.
- ☐ I am comfortable with becoming more physically active on my own without consulting a health care provider or QEP.

Name (+ Name of Parent/Guardian if applicable) [Please print]	Signature (or Signature of Parent/Guardian if applicable)	Date of Birth

Date	Email (optional)	Telephone (optional)

With planning and support you can enjoy the benefits of becoming more physically active. A QEP can help.

☐ Check this box if you would like to consult a QEP about becoming more physically active.
(This completed questionnaire will help the QEP get to know you and understand your needs.)

(141)

APPENDIX B: THREE-FACTOR EATING QUESTIONNAIRE REVIED 18 (TFEQ-R18): RESTRAINED EATING SUBSCALE

Name: Date:

1. I deliberately take small helpings as a means of controlling my weight
   - Definitely True
   - Mostly True
   - Mostly False
   - Definitely False
2. I consciously hold back at meals in order to not gain weight
   - Definitely True
   - Mostly True
   - Mostly False
   - Definitely False
3. I do not eat some foods because they make me fat
   - Definitely True
   - Mostly True
   - Mostly False
   - Definitely False
4. How frequently do you avoid "stocking up" on tempting foods?
   - Almost never
   - Seldom
   - Usually
   - Almost always
5. How likely are you to consciously eat less than you want?
   - Unlikely
   - Slightly likely
   - Moderately likely
   - Very likely
6. On a scale of 1 to 8, where 1 means no restraint in eating (eating whatever you want, whenever you want it) and 8 means total restraint (constantly limiting food intake and never "giving in"), what number would you give yourself?
   - 1
   - 2
   - 3
   - 4
   - 5
   - 6
   - 7
   - 8

Adapted from (142)

APPENDIX C: HEALTH SCREENING FORM

HEALTH SCREENING FORM

The purpose of this form is to ensure that you do not have any health concerns that are contraindications to fitness testing or participation in this study. All results are strictly confidential.

Name: Date:

1. Have you gained or lost greater than 2 kg (~4.4 lbs) within the previous three months?

Yes

No

2. Are you currently attempting to gain or lose weight?

Yes

No

3. Have you started taking an oral contraceptive within the previous three months?

Yes

No

4. Have you had a menstrual cycle within the last 12 months?

Yes

No

Notes:

APPENDIX D: GODIN'S LEISURE TIME EXERCISE QUESTIONNAIRE

Godin's Leisure Time Exercise Questionnaire

We would like you to recall your *average weekly exercise* over the *PAST MONTH*. How many times per week on average did you do the following kinds of exercise over the past month?

When answering these questions please remember to:

- Consider your average over the **past month**
- Only count exercise sessions that lasted ***15 minutes or longer*** in duration
- Only count exercise that was done during **free time** (i.e., do not included occupation or housework)
- Note that the main difference between the three categories is the **intensity** of the exercise
- Write the average frequency on the first line and the average duration on the second line – please write "0" in each line if it does not apply

A. STRENUOUS EXERCISE (Heart beats rapidly, sweating)

(e.g., running, jogging, hockey, soccer, squash, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling, vigorous aerobic dance classes, heavy weight training)

In an average week I was involved in strenuous exercise _____ times/week for an average duration of _____ minutes/each session.

B. MODERATE EXERCISE (Not exhausting, light perspiration)

(e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing)

In an average week I was involved in moderate exercise _____ times/week for an average duration of _____ minutes/each session.

C. MILD EXERCISE (Minimal effort, no perspiration)

(e.g., easy walking, yoga, archery, fishing, bowling, lawn bowling, shuffleboard, horseshoes, golf, snowmobiling)

In an average week I was involved in mild exercise _____ times/week for an average duration of _____ minutes/each session.

Adapted from (145)

APPENDIX E: INFORMED CONSENT FORM

University of Lethbridge
Faculty of Arts & Science

Department of Kinesiology & Physical Education
4401 University Drive Lethbridge, Alberta, Canada T1K 3M4
Phone 403.329.2680 Fax: 403.380-1839

CONSENT TO PARTICIPATE IN RESEARCH
LETTER OF INFORMATION

TITLE: **Prolonged impact of aerobic exercise on appetite and energy intake**

You are being invited to participate in a research study conducted by Tetsuro Okada (MSc Student) from the Exercise and Nutrition Research Laboratory in the Department of Kinesiology and Physical Education.

PURPOSE OF THE STUDY
The goal of the study is to determine the prolonged, 3-day appetite and energy intake response following an aerobic exercise session.

PROCEDURES
Before you participate in this study, you will be asked to complete a health screening form, eating habit questionnaire (TFEQ-R18), and Get Active Questionnaire (GAQ). As the purpose of the GAQ is to ensure that you can safely participate in the study, it is important that you fill out the GAQ form honestly. Beyond the initial screening questions, it is important for you to consider whether this is a study that you would like to participate in given the procedures used. You will be asked to complete an initial 'test trial', where you will be provided a day's worth of the liquid meal-replacement beverage. The initial 'test trial' is intended to give you an idea of what the meal-replacement beverage is like, and whether you think you can sustain the consumption of this diet for four consecutive days, on two different occasions. If you believe that you can adhere to the diet for the entirety of the study, you will be required to complete an initial baseline session and two, 4-day trials. For the initial session, you will be asked to visit the Exercise and Nutrition Research Laboratory at the University of Lethbridge to record measures of height and weight and perform a maximal oxygen consumption (VO_2max) test. The VO_2max will require you to run against a constantly increasing workload until you reach your limit of tolerance and are unable to continue exercising because the intensity is too high or uncomfortable. For the two trials, you will be required to exclusively consume a meal replacement beverage, one fibre bar per day, and bottled water for a period of 4 days. The meal-replacement beverage, fibre bars, and bottled water will be provided to you free of charge. On day 2 of each trial, you will be required to visit the laboratory to complete a 75 min vigorous intensity exercise session on a treadmill or a 75 min sedentary session, where you can complete homework, read, or anything physically inactive within the laboratory. You will provide a small blood sample (6mls) drawn from your forearm at 5 different times throughout each trial (Day 2- before completing the exercise/sedentary session, Day 2 -immediately after the exercise/sedentary session, Day 2 - 1hr post exercise/sedentary session, Day 3 – in the morning, and Day 4 – in the morning). All blood samples will be collected at the Exercise and Nutrition Lab at the University of Lethbridge. Given that you have ~5000ml of blood in your body, the maximum of 30ml of blood collected for each trial represents less than 1% of your blood volume. The blood samples will allow for the measurement of hormones that regulate appetite. During each 4-day trial, you will be required to complete 14 short (1-2 minute) surveys asking you questions about your appetite and hunger. Upon the completion of each trial, you will return all used and unused bottles of the meal-replacement beverage and water to the laboratory. Each trial will be separated by a period of 2-4 weeks.

EXPECTED LENGTH OF PARTICIPATION

Taking into account the two experimental sessions, it is estimated that you will dedicate ~ 10 hours within the Exercise and Nutrition Laboratory, while on a meal-replacement beverage diet for 8 total days, over a 4-8 week period for this study.

POTENTIAL RISKS AND DISCOMFORTS

As the exercise involves stationary running at maximal and submaximal level of intensity there is some risk of injury. You may feel some discomfort while completing the exercise session and there is also a possibility of mild muscle soreness and/or fatigue typical of an intense exercise session. You may also experience some minor discomfort wearing the breathing mask for the VO_2 measurements. With intense exercise, there is a small risk of an acute cardiovascular event (e.g. heart attack, dysrhythmias, etc.). All researchers are trained in Standard First Aid and CPR and automated external defibrillators (AED) are located nearby the laboratory in the case of emergency situations.

Blood sampling may cause some minor discomfort and bruising. All blood samples will be collected under sterile conditions by a researcher who has successfully completed a phlebotomy training course through Bow Valley College (BVC, Calgary, AB).

You may also find that the liquid diet affects your normal feelings of satiety. For this reason, we have included the initial trial period to see if you can tolerate the almost exclusive liquid diet. The only solid food that is permitted during the study period is one provided fiber bar per day. You will still be free to consume coffee and tea, granted that the you do not add anything to these beverages apart from the meal-replacement beverages that you are provided with. The consumption of alcohol is not permitted during the study period. If you cannot tolerate the diet, you are free to withdraw from the study at any point.

POTENTIAL BENEFITS TO PARTICIPANTS AND/OR SOCIETY

With your participation in this study you will complete maximal and submaximal exercise session which will provide you with information regarding your VO_2max, heart rate, and workload. Additionally, this study may provide you with insight into how your eating behaviour is affected by an acute bout of aerobic exercise. You are encouraged to ask questions regarding the purpose of the study, specific measures or outcomes of your exercise test, or overall findings and conclusions from the research study.

CONFIDENTIALITY

Only researchers associated with this study will have access to any identifying information. The researchers associated with the study will all sign a confidentiality agreement. Identifying information will be collected on a master list that will be kept in a password-protected file that can only be accessed by study investigators. For data analysis, all participants will be assigned an arbitrary number to ensure anonymity. Any published data will contain only the number of participants of each sex and the average values for each experimental trial. All data will be presented in terms of averages, percentages, and ratios. Academic publications and presentations resulting from this study will not identify you by name.

COMPENSATION

You will receive $50 for participating in a trial, for a total of $100 for participating in both experimental trials. There will be no compensation for participating in the baseline VO_2max testing.

PARTICIPATION AND WITHDRAWAL

Your participation in this research study is completely voluntary. You may withdraw at any time without consequence by calling or emailing Tetsuro Okada (403-998-9217, tetsuro.okada@uleth.ca) or Marc Bomhof (403-332-4437, marc.bomhof@uleth.ca). If you are a student who chooses to withdraw, it will not affect your status at the University of Lethbridge. Apart from the questions within the GAQ, you may refuse to answer any questions you feel are inappropriate and still remain in the study. Upon withdrawal, you may choose if any data collected from you is to be kept for analysis, or if you would like to remove it

from the study. The investigators may withdraw you from this research if circumstances arise which warrant doing so.

FEEDBACK OF THE RESULTS OF THIS STUDY

If you would like a copy of your personal results and/or a copy of the overall study findings, please check the box below. Personal results will include a summary of your cardiovascular fitness parameters from the VO_2max as well as information about your energy intake and energy expenditure between the two, 4 day trials. The overall study findings will be reported in the form of speech, manuscripts (written reports), or poster presentations given at scientific meetings. The information published in a journal or subsequent studies will not identify you in any way. Copies will be available upon request by checking the box(es) below.

☐ Personal Results ☐ Overall Study Findings

RE-RECRUITMENT IN FUTURE STUDIES

If you check the box below, you consent to be contacted regarding potential participation in future studies in the Exercise and Nutrition Research Laboratory. We will contact you with information and the option to participate if you choose.

☐

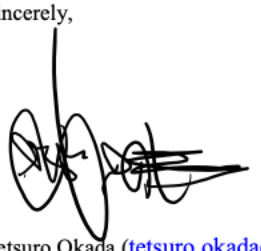
IF I SUFFER A RESEARCH-RELATED INJURY, WILL I BE COMPENSATED?

In the event that you suffer injury as a result of participating in this research, you will receive necessary medical treatment, at no additional cost to you. By signing this consent form, you are not releasing the investigator, his supervisor, or the institution from their legal and professional responsibilities.

This letter is yours to keep. If you have any questions about this research project, please call: Tetsuro Okada (403-998-9217) or Dr. Marc Bomhof (403-332-4437).

Further, if you have any questions about the conduct of this study or your rights you may contact the Office of Research Ethics at the University of Lethbridge at 403-329-2747, or email via research.services@uleth.ca

Sincerely,



Tetsuro Okada (tetsuro.okada@uleth.ca), Student Investigator

Dr. Marc Bomhof (marc.bomhof@uleth.ca), Principal Investigator

Consent Statement

Title of Study: **Prolonged impact of aerobic exercise on appetite and energy intake**

MSc Student Investigator: Tetsuro Okada **Phone Number:** (403) 998-9217
Faculty Supervisor: Dr. Marc Bomhof **Phone Number:** (403) 332-4437

	Yes	No
Do you understand that you have been asked to be in a research study?	☐	☐
Have you read and received a copy of the attached Letter of Information?	☐	☐
Do you understand the benefits and risks involved in taking part in this research study?	☐	☐
Have you had an opportunity to ask questions and discuss this study?	☐	☐
Do you understand that you are free to leave the study at any time, without having to give a reason?	☐	☐
Has the issue of confidentiality been explained to you?	☐	☐
Do you understand who will have access to your information?	☐	☐
Who explained this study to you? _____		
Sex: ☐ Male ☐ Female ☐ Prefer not to say		

By signing below, I agree to participate in this study

_____

Participant's Name Signature Date

_____

Investigator's Name Signature Date

APPENDIX F: 100 MM APPETITE VISUAL ANALOGUE SCALE (VAS)

Appetite VAS

I am not hungry at all	How hungry do you feel?	I have never been more hungry
I am completely empty	How satisfied do you feel?	I cannot eat another bite
Not at all full	How full do you feel?	Totally full
Nothing at all	How much do you think you can eat?	A lot
Yes, very much	Would you like to eat something sweet?	No, not at all
Yes, very much	Would you like to eat something salty?	No, not at all
Yes, very much	Would you like to eat something savoury?	No, not at all
Yes, very much	Would you like to eat something fatty?	No, not at all

Adapted from 153