Behavioural compensatory and metabolic changes in response to exercise in overweight and obese women

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ABSTRACT

This thesis describes the behavioural compensatory responses and metabolic changes in response to a single exercise session and training programmes in overweight and obese women and consists of a literature review (Chapter 1), a general methods chapter (Chapter 2), three experimental chapters (Chapter 3- Chapter 5) and a general discussion and conclusions chapter (Chapter 6).

Experimental chapter 3 presents a study which aimed to investigate the impact of a single moderate-intensity cycling exercise session with energy expenditure of approximately 2 MJ on appetite measures, energy intake and metabolic variables in response to four *ad libitum* meals in overweight and obese females. Twelve sedentary, overweight and obese women underwent one exercise and one control trial each over two consecutive days. Appetite and metabolic variables such as glucose, insulin and triglycerides were measured frequently and four buffet meals were served throughout each trial. The findings suggest that a single exercise session performed by overweight and obese women does not elicit compensatory responses in appetite and energy intake and reduces triglyceride concentration by 17% in response to an *ad libitum* breakfast consumed 14 hours after exercise.

Chapter 4 aimed to examine the extent to which changes in physical activity outside of the exercise intervention and energy intake contribute to individual differences in body fat loss induced by exercise training programmes. To determine this, thirty-four overweight and obese sedentary women participated in a structured and supervised 8-

week exercise programme consisting of 150 minutes of cycling exercise per week. Body composition, total energy expenditure and components such as exercise, activity, sedentary and sleeping energy expenditure as well as energy intake from 7-day weighed intake were determined before and during the last week of the exercise intervention. The findings indicate that overweight and obese women who during exercise intervention achieve lower than predicted fat loss are compensating by being less active outside exercise sessions.

The aim of Chapter 5 was to investigate how physical, fitness and metabolic characteristics of overweight and obese women are influenced by two 8-week supervised aerobic exercise programmes with exercise sessions conducted twice per week for the duration of 75 minutes and with exercise sessions conducted 5 times per week for the duration of 30 minutes. Thirty-four women were randomised into either long and less frequent or short and more frequent cycling exercise groups. Body composition, fitness and metabolic variables were measured prior and after the intervention. The findings indicate that frequency and duration of exercise sessions does not alter the effects of an exercise programme on health related outcomes which were evident in the absence of weight loss, when the total volume of exercise undertaken is the same.

Based on obtained data the following conclusions have been drawn:

Overweight and obese women do not compensate in terms of appetite and energy intake for the energy expended in a single exercise session, when this is in line with

recommended expenditure for individual exercise sessions aimed at body weight and body fat reduction.

Compensatory responses in terms of changes in energy intake are also not evident in overweight and obese women participating in an 8-week exercise training programme. However, predicted body fat loss can be expected to match the amount of fat actually lost only in those who do not decrease physical activity outside exercise sessions.

A single exercise session with energy expenditure similar to that recommended for individual exercise sessions aiming at body mass and body fat reduction, reduced triglyceride concentration by 17% in response to an *ad libitum* breakfast consumed 14 hours after exercise.

Changes in fitness, insulin resistance, diastolic blood pressure and waist circumference in sedentary overweight and obese women induced by an 8-week exercise programme incorporating 150 minutes of exercise per week are independent of frequency and duration of exercise sessions with 2 x 75 minute exercise sessions per week and 5 x 30 minute exercise sessions per week eliciting similar changes.

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AUTHOR'S DECLARATION

I declare that the work contained in this thesis is original, and is the work of one author, Eirini Manthou except where otherwise stated. The information reported from other authors has been quoted with their name and source of publication. The relative contributions in terms of study design, data collection and analysis have been highlighted at the beginning of each research chapter.

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ἐὰν ταῖς γλώσσαις τῶν ἀνθρώπων λαλῶ καὶ τῶν ἀγγέλων, ἀγάπην δὲ μὴ ἔχω, γέγονα χαλκὸς ἠχῶν ἢ κύμβαλον ἀλαλάζον…

(Απ. Παύλου, Α' Κορ.ιγ΄)

if I speak in the tongues of all men and even angels, but I have not love, I resemble a noisy gong or a clanging cymbal…

(Apost. Paul, A' Cor. ιγ΄)

«Που πάμε; Μη ρωτάς! Ανέβαινε, κατέβαινε. Δεν υπάρχει αρχή, δεν υπάρχει τέλος. Υπάρχει η τωρινή στιγμή, γιομάτη πίκρα, γιομάτη γλύκα και τη χαίρουμαι ούλη!»

(Νίκος Καζαντζάκης, Ασκητική)

“Where do we go? Don’t ask! Ascend, descend. There is no beginning, no end. There exists only this moment, full of bitterness, full of sweetness and I relish it ALL!”

(Nikos Kazantzakis in “The Saviours of God”)

DECLARATION OF PUBLICATIONS

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LIST OF ABBREVIATIONS

BMI	**Body Mass Index**
FTO	**Fat Mass and Obesity Associated gene**
EE	**Energy Expenditure**
DLW	**Doubly Labelled Water**
CVD	**Cardiovascular Disease**
NHANES	**National Health and Nutrition Examination Survey**
NEAT	**Non-Exercise Activity Thermogenesis**
HR	**Heart Rate**
CHD	**Coronary Heart Disease**
ACSM	**American College of Sports Medicine**
AHA	**American Heart Association**
ExEE	**Exercise Energy Expenditure**
CDC	**Centers of Disease Control**
WHO	**World Health Organisation**
IOM	**Institute of Medicine**
CMO	**Chief Medical Officer**
NIH	**National Institute of Health**
PAL	**Physical Activity Level**
REI	**Relative Energy Intake**
DTE	**Desire to Eat**
PFC	**Prospective Food Consumption**
RQ	**Respiratory Quotient**

TEE	**Total Energy Expenditure**
VO_{2max}	**Maximum Oxygen Uptake**
ICAM-1	**Intercellular Adhesion Molecule-1**
VCAM-1	**Vascular Cell Adhesion Molecule-1**
NO	**Nitric Oxide**
NEFA	**Non-esterified Fatty Acids**
TG	**Triglycerides**
VLDL	**Very Low Density Lipoprotein**
FFA	**Free Fatty Acids**
GLUT-4	**Glucose transporter type 4**
β-HAD	**β-Hydroxybutyrate**
LDL	**Low Density Lipoprotein**
HDL	**High Density Lipoprotein**
LPL	**Lipoprotein Lipase**
CRP	**C-Reactive Protein**
TNF-α	**Tumor Necrosis Factor- α**
IL-1β	**Interleukin-1β**
IL-6	**Interleukin-6**
IL-1	**Interleukin-1**
RMR	**Resting Metabolic Rate**
VO_2	**oxygen uptake**
VCO_2	**carbon dioxide production**
HR_{max}	**Maximum Heart Rate**

LT	**Lactate Threshold**
LDH	**Lactate Dehydrogenase**
RPE	**Rate of Perceived Exertion**
AEE	**Activity Energy Expenditure**
SEDEE	**Sedentary Energy Expenditure**
SEE	**Sleeping Energy Expenditure**
ELISA	**Enzyme-linked Immunoassay**
TMB	**3,3',5,5'-Tetramethylbenzidine**
NAD^+	**Nicotinamide Adenine Dinucleotide**
ANOVA	**Analysis of Variance**
$HOMA_{IR}$	**Homeostasis Model Assessment of Insulin Resistance**
EDTA	**Ethylenediamine Tetra-Acetic Acid**
CHO	**Carbohydrates**
AUC	**Areas Under Curve**
LB	**Long Bouts**
SB	**Short Bouts**

Chapter 1: Introduction and Literature Review

1.1 Introduction

This chapter aims to provide evidence of the relevant scientific background of the studies contained in this thesis and to establish the theoretical basis for these studies. First of all the epidemic of obesity is described and an overview of physical activity recommendations is presented with special emphasis to recommendations directed to health benefits and weight management. Then acute, medium and long term exercise studies are considered in relation to changes in appetite, energy balance and impact on metabolic risk factors for cardiovascular disease and type 2 diabetes.

1.2 Obesity: prevalence, aetiology and associated comorbidities

The prevalence of overweight and obesity worldwide is ever increasing (Ford and Mokdad, 2008) and apart from the health detriments it exerts a huge economic burden on individuals and national health care systems (Müller-Riemenschneider, 2008). In 2005, 1.5 billion people had body mass index (BMI) > 25 $kg \cdot m^{-2}$ and 300 million people had BMI > 30 $kg \cdot m^{-2}$ globally (Haslam et al., 2005). According to the latest National Health and Nutrition Examination Survey (NHANES, 1999-2008) the prevalence of obesity in US in 2007-2008 was 32.2% among adult men and 35.5% among adult women and although the increase does not follow the pace of previous decades is still high (Flegal et al., 2010). Additionally, the prevalence estimates for overweight and obese combined were 68% over the whole US population (Flegal et al., 2010). Obesity prevalence in the European region, although much lower than in US, differs highly

among countries. In general, 4.0%-28.3% of men and 6.2%-36.5% of women are categorized as obese, with overall prevalence rates being higher in Central, Eastern and Southern countries than those in Western and Northern European countries (Berghöfer et al., 2008). In 2005 it was stated that obesity prevalence in England almost tripled in the time course of two decades (Katz et al., 2005). The Annual Statistical Report from the National Health System estimated that in 2008 almost 24% of men and 25% of women in England were classified as obese (NHS, 2010). According to the Scottish Health Survey, in 2008 almost two-thirds of men (68.5%) and women (61.8%) were overweight and obese. Between 1995 and 2008 there was an almost 10% increase amongst those who were obese; the percentage for obese men increased from 16% to 26% and from 17% to 27.5% for obese women (The Scottish Health Survey, 2009). Since recent data show that obesity is 1.5 to 2 times higher in women than men in most countries around the world (Lovejoy et al., 2008), overweight and obese women constitute a population in need of special attention from health professionals.

Although the aetiology of obesity is not fully understood, heredity and/ or behaviour have been postulated among other possible factors as main contributors to the increase of obesity (Bleich et al., 2008; Keith et al., 2006). The genetic factors predisposing to obesity are poorly understood and the attempt to associate candidate "obesity genes" with human adiposity have been relatively unsuccessful in the past (Loos and Bouchard., 2003). Recently, however, geneticists identified variants (Frayling et al., 2008) and high-risk, high-penetrant genotypes (Walters et al., 2010), which are common among the obese. For instance, the fat mass and obesity associated (FTO) gene has been found to

predispose to obesity (Frayling et al., 2008). Interestingly, the FTO variant has not been linked with the regulation of energy expenditure (EE) but it is believed to have a role in the control of food intake and food choice (Cecil et al., 2008). However, a recent study has shown that adolescents who meet the daily physical activity recommendations (i.e. ≥ 60 minutes of moderate to vigorous exercise per day) may overcome the effect of the FTO polymorphism on obesity compared with those who do not (Ruiz et al., 2010). This evidence suggests that heredity and behaviour may exert an independent or combined effect on the development of obesity; however direction of causality is still difficult to be determined.

The rapid weight gain seen in recent years, potentiate behaviour as a major contributor to energy imbalance. Energy intake and EE spent in physical activity are regarded as the two major behavioural determinants of body weight contributing to the obesity epidemic (Lau et al., 2007). The readily available energy-dense foods combined with the increasingly sedentary lifestyle employed in Western Society are two key components that are thought to be largely responsible for the common transition into positive energy balance (Martins et al., 2008). Ecological evidence suggests that increasing prevalence of obesity has occurred simultaneously with changes in physical activity patterns, therefore it could be inferred that obesity is attributable to reduced EE that has not been matched for by an equivalent decline in energy intake (Fox and Hillsdon, 2007; Jebb and Moore, 1999; Prentice and Jebb, 1995). Data from National Health Surveys have detected minimal changes in caloric intake at present in comparison to 20 years ago (Department for Environment Food and Rural Affairs, 2007), leading to the view that a

reduction in physical activity may play a central role in the aetiology of obesity. In contrast, MONICA project examining the relationship between secular trends in energy supply and BMI among several countries revealed that increasing energy supply is closely associated with the increase of overweight and obesity in western countries (Silventoinen et al., 2004).

However, this kind of evidence does not provide as high a level of causal inference as data at an individual level (Wareham, 2007). To address this issue, a study looked at the amount of EE spent in physical activity over the past 25 years in 393 individuals from US and 366 from Maastricht using the doubly-labelled water (DLW) method (Westerterp and Speakman, 2008). By comparing total daily EE in the early 1980s with current data the researchers suggested that there has been no significant decline in the energy individuals expended through physical activity, suggesting that increased energy intake might be the major contributing factor in the disrupted energy balance equation (Westerterp and Speakman, 2008). The accumulating data from DLW studies show that emphasis of research should be placed on identification of mechanisms underlying the mismatch between energy intake and expenditure (Schoeller, 2008).

Obesity is associated with several comorbidities that significantly increase the morbidity and mortality risk (Flegal et al., 2005). Complications are either directly caused by obesity or indirectly related to mechanisms sharing a common cause such as unhealthy diet or sedentary lifestyle and can be categorised to those attributed to increased fat mass such as osteoarthritis and obstructive sleep apnea, and those attributed to increased

number of fat cells such as diabetes, cancer, cardiovascular disease and non-alcoholic fatty liver disease (Haslam and James, 2005). It is widely accepted that high levels of adiposity increase the risk of metabolic disorders such as insulin resistance, hypertension, dyslipidaemia, hypercoagulation, inflammation and impaired vascular function, which are risk factors for chronic disease such as type 2 diabetes and cardiovascular disease (CVD) (Grundy, 2004). Accumulating data suggest that regional fat distribution substantially affects the incidence of comorbidities. High abdominal fat content and waist circumference over 102 cm in men and 88 cm in women is strongly correlated with worsened metabolic and clinical consequences of obesity (Wijga et al., 2010; Katzmarzyk et al., 2006, Després and Lemieux, 2006). Although a cause-and-effect relationship of increased obesity and related comorbidities is not exhaustively demonstrated, a large percentage of CVD and type 2 diabetic patients are obese (Seidell, 2005).

Management of overweight and obesity is highly prioritised by public health initiatives nowadays, because numerous studies have shown that formerly obese individuals who lose weight may substantially reduce blood pressure (Neter et al., 2003; Lalonde et al., 2002; Stevens et al., 2001), inflammatory markers (Kopp et al., 2003; Tchernof et al., 2002; Heilbronn et al., 2001) and improve glucose tolerance (Flechtner-Mors et al., 2000; Ditschuneit et al., 1999) and dyslipidaemia (Lalonde et al., 2002; Dattilo et al., 1992; Wadden et al., 1999). Far more evidence proves the effectiveness of activity/cardiorespiratory fitness on metabolic health benefits (Oguma et al., 2004; Williams et al., 2001; Blair et al., 2001; Blair et al., 1996) even in the absence of weight

loss (Lloyd-Jones et al., 2007; Katzmarzyk et al., 2005; Lee et al., 1999). Given that exercise has a possible role in weight management in addition to the recognised beneficial effect of increased physical activity/ fitness on metabolic profile, various official bodies were directed to formulate and provide the public with physical activity recommendations.

1.3 Physical activity recommendations

Physical activity promotion was always present across history and cultures, resulting in current attitudes and guidelines. Earlier though, the role of physical activity was central and naturally incorporated in every day life (Eaton et al., 1988). The first person in history to provide the public with advice for maintaining health through regimen was Hippocrates (470BC-410BC) who wrote that "all parts of the body which have a function, if used in moderation and exercised in labours in which each is accustomed, become thereby healthy, well-developed and age more slowly, but if unused and left idle they become liable to disease, defective in growth and age quickly" (Jones, 1967).

In modern days, research work to elucidate a possible relationship between physical activity and health only started in early 1950's. Pionneering studies by Morris and colleagues (1953) showed much lower rates of coronary heart disease (CHD) and death due to heart attack among the physically active bus conductors than among the sedentary bus drivers. Based on those findings the hypothesis that increased physical activity protects against CHD was formulated. More studies followed afterwards, among which a study of the relationship of physical activity at work to CHD deaths in US longshoremen

(Paffenbarger and Hale, 1975). This research provided further strong evidence of the benefits of physical activity. After a considerable amount of literature was collected the American College of Sports Medicine (ACSM) published for the first time in 1975 the book "Guidelines for Graded Exercise Testing and Exercise Prescription". This book primarily included recommendations for the frequency, intensity and duration of exercise specified in the context of cardiac rehabilitation (ACSM, 1975). Revised editions of this book followed afterwards and had a major influence on the fields of exercise science and medicine. It is remarkable that all editions focused mainly on the amount of exercise required to improve and maintain physical fitness rather than addressing the relationship between physical activity and health (ACSM, 1978; ACSM, 1980; ACSM, 1986; ACSM, 1991; ACSM, 1998). In those guidelines physical activity was defined as "any bodily movement" and exercise as "a subset of physical activity that is characterised by planned and purposeful training" (Caspersen et al., 1985), which definitions are currently used to distinguish exercise from overall physical activity. It was only in 1992, when the American Heart Association (AHA) released a report that identified physical inactivity as the fourth major modifiable CHD risk factor, joining smoking, hypertension, and dyslipidaemia. An important feature of this report was the recognition of the value of moderate amounts and intensities of physical activity for health. Evidence cited in the report supported the conclusion that there was an inverse and graded dose-response association between physical activity and CHD, but high levels of training were not required for a person to gain much of the health-related benefit of physical activity (Fletcher, 1992).

The use of self-reported physical activity by early epidemiological studies, led to large amount of misclassification and subsequently underestimation of the observed effect. A study by Blair and colleagues (1996) illustrated that objectively measured low cardiorspiratory fitness was a predictor of CVD death rates among women and men. Especially notable was the very large difference in CVD death rates between the low fit and the moderately fit group implying that moderately fit individuals achieved considerably larger benefit against CVD death rates in comparison to their unfit counterparts. Since then, increased physical activity and/or cardiorespiratory fitness levels has been repeatedly demonstrated to be inversely related to CVD risk (Oguma et al., 2004; Williams et al., 2001; Blair et al., 2001). In addition, it was shown that overweight and obese individuals who lead an active lifestyle and/or have high cardiorespiratory fitness are likely to exhibit much lower metabolic risk than their inactive counterparts or the same metabolic risk as inactive or unfit individuals of normal weight (Katzmarzyk et al., 2005; Lee et al., 1999). This is an extremely important finding, which suggests that even in the absence of weight loss, physical activity has the potential to modulate metabolic risk in overweight and obese individuals.

A dose-response relationship between physical activity and all-cause morbidity and mortality was widely demonstrated and is especially relevant to CVD and type 2 diabetes risk reduction. A report from the Nurses' Health Study (Whang et al., 2006) showed a substantial decrease in the age-adjusted hazard ratio for sudden cardiac death among women who spent more than 3.9 hours per week in moderate to vigorous

physical activity assessed by questionnaires. Barlow and colleagues (2006) reported that after adjusting for age and other relevant factors, the risk of developing hypertension was markedly decreased for women who were moderately fit and even further decreased for women who were highly fit. Physical activity is also shown to attenuate adverse effects in the progression from normoglycaemia to clinical type 2 diabetes and the various complications in a dose-response manner (La Monte et al., 2005). The Diabetes Prevention Study in Finland (Tuomilehto et al., 2001; Eriksson et al., 1999) and the Diabetes Prevention Programme in US (Knowler et al., 2002) provide strong evidence that intensive lifestyle modifications, including diet and physical activity considered together or independently, reduce the risk of developing type 2 diabetes. According to the Nurse's Health Study (Hu et al., 1999) the IOWA Women's Health Study (Folsom et al., 2000) and the study of Eastern Finns (Hu et al., 2003) approximately 30 minutes of physical activity of moderate intensity at least 5 days per week provides a substantial 25-36% risk reduction in type 2 diabetes.

From all accumulating findings it is evident that increased levels of physical activity essentially prevent chronic disease and premature death. However, the optimal volume and the exact characteristics of planned exercise such as frequency, exercise programme and session duration and intensity of exercise in order to obtain health benefits are still under debate. Data on intensity and volume of activity were accumulated from early observational studies that have shown a significantly lower death rate from CHD and greater life expectancy of 1 to 2 years by the age of 80 in people who perform an average of 47 minutes versus 15 minutes of activity per day, (Leon et al., 1987) and in men who

expend an estimated 2000 kcal (~ 8.4 MJ) or more per week versus those who expend 500 kcal (~ 2.1) or fewer per week (Paffenbarger et al., 1986). The nature of the most frequently reported activities in those studies suggests that it is unlikely that most of the activities were performed continuously but it is more possible that they reflect accumulation of activity, most of which was performed intermittently (Pate et al.,1995). Studies to address the effects of continuous versus intermittent activity on fitness concluded that both modalities would exert the same impact on fitness (DeBusk et al., 1990; Ebisu et al., 1985). In addition, it was found that moderate-intensity exercise (≥ 5.5 METs for at least 40 minutes per week) and cardiovascular fitness of more than 31 $ml \cdot kg^{-1} \cdot min^{-1}$ $\dot{V}O_2$ effectively prevent against type 2 diabetes (Lynch et al., 1996). Subsequent studies have shown that even an average exercise energy expenditure (ExEE) of about 1000 kcal (~ 4.2 MJ) per week over-and-above other activity is associated with a 20%–30% reduction in all-cause mortality (Lee et al., 1999; Paffenbarger et al., 1993). If this amount of weekly EE is allocated equally to the most days of the week would equal ExEE of 200 kcal (~ 0.8 MJ) on five days of the week. Evidence was thus mounting that vigorous or continuus exercise was not necessarily needed for someone to acquire health benefits. Subsequently, a 'public health prescription' advocating moderate physical activity came into light in 1995. The American Centers for Disease Control and Prevention (CDC) and the ACSM co-published a landmark report emphasising the accumulation of 30 minutes or more of moderate-intensity physical activity on most, preferably all, days of the week (CDC/ACSM, 1995), (Pate et al., 1995). This amount would be equivalent to 150-200 kcal (~ 0.6-0.8 MJ) per day depending on individual body mass (Saris et al., 2003). Other

similar recommendations followed from the US Surgeon General (US Surgeon General, 1996), the National Institutes of Health (NIH) (NIH, 1996) and the World Health Organization (WHO) (WHO, 1995). Those reports mainly drew attention to health benefits acquisition, through the amount of physical activity that was widely interpreted as “30 minutes on five days of the week”. The recommendations were distinct in two important ways. First, the health benefits of moderate-intensity regular physical activity were identified. Second, it was revealed that accumulation of physical activity of the recommended amount of exercise could be achieved through intermittent, short bouts. It was finally concluded by the works panel that a simple message as “30 minutes on five days of the week” might be easier interpreted and reach the public and thus greater number of individuals would probably adhere to such activities that could be performed even outside formal exercise programmes. While the amount of physical activity suggested in those recommendations were agreed as an adequate dose for general health promotion and disease prevention (Erlichman et al., 2002), several reports have questioned whether they were sufficient to promote weight loss and prevent unhealthy weight (re)gain (Schoeller et al., 1997).

Under the pressure of the rising obesity trends, official bodies were promted to recommend a dose of physical activity that would be effective in weight management. That essentially meant that the optimum and minimum amount of physical activity and components to help in weight reduction, weight maintenance after weight loss and prevention of weight gain were sought. Physical activity EE represents the most variable component of TEE accounting for 15-30% of the daily EE. It can be subdivided into

volitional exercise (sports and fitness-related activities) thermogenesis and non-exercise activity thermogenesis (NEAT). Non-exercise activity thermogenesis - a term coined in 1999 by Levine et al. - includes all activities that do not fall into the category of volitional exercise, such as the activities of daily living, fidgeting, spontaneous muscle contraction and posture maintenance. It has been suggested that NEAT may account partly for the recent increase in the obesity epidemic as obese individuals appear to be 2.5 hours more sedentary than their lean counterparts. Non-exercise activity thermogenesis is highly variable between individuals, however it is quite difficult to be determined precisely and physical activity recommendations do not address this matter directly.

In 1998 and 2001 the American National Heart, Lung and Blood Institute and the ACSM have published physical activity recommendations for weight loss. These positions state, "For long term weight loss, overweight and obese adults should progress to 200-300 minutes of moderate intensity exercise per week, or 2000 kcal (~ 8.4 MJ) per week of leisure type physical activity" (Jakicic et al., 2001). However this statement was not very understandable for the public as it would appear that physical activity and exercise can be used interchangeably and are synonymous. Apart from that, it was limited to weight loss in overweight and obese adults.

In 2002, recommendations on dietary reference intakes from the American Institute of Medicine (IOM) panel were released. Recognising that physical activity is an important part of wellbeing and weight management the IOM report included the comment that

previous recommendations (30 minutes per day of regular activity) are insufficient to maintain body weight in adults in the recommended BMI range of 18.5 up to 25 $kg \cdot m^{-2}$ and to achieve all the identified health benefits fully. Hence, to prevent weight gain as well as to accrue additional, weight-independent health benefits of physical activity, 60 minutes of daily moderate-intensity physical activity (e.g. walking/jogging at 4 to 5 mph) was recommended (IOM, 2002).

The overall consensus that physical activity of 60 minutes on 5 days of the week is required for obesity management purposes was supported by a pool of evidence examined meticulously. Many population studies have shown that measures of body fat levels are lower in those individuals who undertake more physical activity. For example, data from a population study showed that BMI, percentage of body fat and waist to hip ratio appeared to be decreased as physical activity levels increased (Holcomb et al., 2004). However, a number of meta-analyses have shown that the amount of weight loss due to increased physical activity levels tends to be small and it is greater for men than for women. Ballor and Keesey (1991) conducted a meta-analysis of exercise and weight loss that included 53 studies, with ExEE of approximately 1500 kcal (~ 6.3 MJ) per week for men and ExEE of more than 900 kcal (~ 3.8 MJ) for women. Mean weight loss for men was approximately 1.4 kg after 16 weeks, while mean weight loss for women was less than 1 kg after 11 weeks. Similarly, a meta-analysis by Garrow and Summerbell (1994) found slightly greater weight loss but difference of the same magnitude between genders.

In a study under supervised conditions, Ross et al., (2000, 2004) found that 500- 700 kcal (~ 2.1- 2.9 MJ) deficit per day either through diet or exercise produced a 6.5% weight loss for women and an 8% weight loss for men over a 12-week period. In a 16-month supervised exercise trial, Donnelly et al., (2003) found that men expended approximately 300 kcal (~ 1.3 MJ) more per session than did the women when prescribed the same relative amount of exercise in terms of frequency, intensity and duration with habitual diet maintenance. Men lost on average 5% of their baseline weight within 9 months in contrast to women who lost little or no weight on average over the 16 months. Individual variability was evident especially in women. Other research evidence showed that either a 12-week exercise trial of 30-60 minutes per day with a low fat diet (Bond et al., 2002) or longer term clinical trials (Jakicic et al., 1999) were rather insufficient to reduce weight in overweight individuals. However, overweight women who maintained an average of more than 280 minutes of exercise per week, consistent with recommendations, over 18 months, lost significantly greater weight than those who undertook 150-200 and less than 150 minutes of exercise per week (Jakicic et al., 1999). It would appear, therefore, that long term weight loss is improved as exercise duration increases, however, response to exercise programmes may be individual and/or gender specific.

In terms of intensity, data from cross sectional studies suggest that high-intensity activities result in greater reductions in body mass and body fat (Coakley et al., 1998; Haapanen et al., 1997); however, data from experimental trials does not support this view. A study examining varying intensities of exercise on changes in body mass and

body composition has demonstrated no effect of exercise intensity in spite of greater improvements in cardiorespiratory fitness with high-intensity exercise (Duncan et al., 1991). To examine the amount and intensity effect of exercise on weight loss, overweight untrained adults undertook an 8-month randomised controlled trial of different exercise doses in the STRIDDE studies (Slentz et al., 2004). Overweight individuals underwent three different exercise trials with no change in habitual diet. The control group gained about 1 kg, the low-amount/ moderate-intensity exercise group (equivalent to 12 miles walking per week) and the low-amount/ vigorous-intensity group (equivalent to 12 miles jogging per week) lost about 1 kg. The high-amount/ vigorous-intensity exercise group (equivalent to 20 miles jogging per week) lost about 3.5 kg or approximately 4% of their body weight, which approaches clinical significance with regard to health benefits. Slentz et al., (2004) examined weight change per mile and suggested that covering a distance of 6 miles per week corresponds with the amount of exercise that results in weight maintenance. Moreover, despite preliminary evidence suggesting that intermittent exercise protocols improved weight loss (Jakicic et al., 1995) subsequent studies have shown no additional benefit in weight loss over an 18-month intervention when comparing continuous exercise with intermittent exercise programmes (Donnelly et al., 2000; Jakicic et al., 1999). Given the limited literature in the effect of exercise programmes of the same EE but different modalities on weight management it would be interesting to investigate the impact of different combinations of frequency, intensity and session duration on exercise adherence and subsequent weight loss. This would probably give further options and flexibility in individuals who

dislike or perceive barriers to current exercise recommendations or would reveal an optimum combination of exercise characteristics for weight management purposes.

Prospective studies conducted in individuals who have lost weight have found improved weight maintenance when exercise was included in a post weight loss programme (Williamson, 1996; Wing, 1992; Pavlou et al., 1989). There appears to be a dose-response relationship between physical activity undertaken and prevention of weight regain with large volumes of physical activity being associated with less weight gain (Fogelholm and Kukkonen-Harluja, 2000). A dose-response effect was demonstrated in a study by Jakicic et al., (1999). After weight loss at 6 months, weight was maintained for 6 months by those exercising more than 200 minutes per week, whereas those exercising less than 150 minutes per week experienced weight regain. Schoeller et al., (1997) showed that moderate-intensity exercise for 65 minutes per day was associated with improved weight maintenance over 1 year. Furthermore, body weight maintainers were reported to have a physical activity level (PAL) (TEE:BMR) of more than 1.75 which corresponds to 80 minutes of moderate-intensity (4 METs) or 35 minutes of vigorous activity (6 METs) per day, whereas regainers had a PAL of 1.5 to 1.6 (Schoeller et al., 1997). Therefore, it appears that persons attempting to maintain a reduced body mass may need to do 60-90 minutes activity per day in order to avoid gaining weight (Elrichman et al., 2002). It is possible that formerly obese individuals need to perform an even greater amount of exercise due to habitually increased energy intake.

The effect of exercise on prevention of weight gain was demonstrated in an 18-month study on middle-aged women. Donnelly et al., (2000) showed that either 30 minutes of supervised continuous exercise 3 times a week or two 10- to 15-minute bouts of supervised exercise 5 times a week prevented weight gain without dietary restriction. Dunn et al., (1999) found that sedentary men and women randomised either to lifestyle or structured exercise groups with a goal of 1000 kcal (~4.2 MJ) of ExEE per week gained little or no weight in the two-year intervention period. This evidence supports the notion that relatively small amounts of physical activity may be sufficient to enable people to prevent unwanted weight gain and that it is rather more realistic for sedentary individuals to initially target adoption and maintenance of lower amounts and then progress to higher amounts of moderate-intensity exercise.

In an effort to harmonise and clarify recommendations on prevention of weight gain the first consensus meeting on recommendations was held in 2003. After the exhaustive examination of related literature it was pointed that the PAL of a regular exerciser is equivalent to 1.75, while the PAL of a sedentary individual is 1.4. The difference between these two PALs equates to an additional 490 kcal (~ 2 MJ) per day for an individual with resting metabolic rate (RMR) of 1400 kcal (~ 5.9 MJ) per day which is far higher than the 150-200 kcal (~ 0.6- 0.8 MJ) per day based on the 30 minutes per day recommendations and would be equivalent to at least double the duration of an exercise session. Therefore, Saris et al., (2003) stated that to prevent weight regain in formerly obese individuals 60-90 minutes of moderate-intensity activity or lesser amounts of daily vigorous-intensity activity are needed. The panel of the consensus statement also

suggested that it is likely that moderate intensity activity of approximately 45 to 60 minutes per day, or PAL of 1.7 is required to prevent the transition to overweight or obesity. In 2004, a report from the Chief Medical Officer (CMO) of UK was published, which contained recommendations for active living throughout the life course. Those recommendations revealed the dual role of exercise to the public in terms of health and weight management. It was stated that for general health benefits, adults should achieve a total of at least 30 minutes a day of moderate-intensity physical activity on 5 or more days of the week, while the recommended levels of activity can be achieved either by doing all the daily activity in one session, or through several shorter bouts of activity of 10 minutes or more. It was additionally suggested that physical activity could be incorporated in daily routine or in structured exercise or sport, or a combination of these. This report made clear to the public that all movement contributes to EE and is important for weight management, as well as it is likely that for many people, 45-60 minutes of moderate-intensity physical activity a day is necessary to prevent obesity. Finally, specific activity recommendations were made for adults with diseases and related conditions; for example activities that produce high physical stresses on the bones were claimed necessary for bone health (CMO, 2004).

In 2007, ACSM and AHA (Haskell et al., 2007) updated and clarified further previous recommendations on the type and amount of physical activity needed by healthy adults to improve and maintain health. In addition to the primary goal of 30 minutes on 5 days each week it was suggested that combinations of moderate- and vigorous-intensity activity can be performed to meet this recommendation. Also moderate and vigorous

activity terms were explained and examples of either type of activity were given. It was stated for example, that moderate-intensity aerobic activity, is generally equivalent to a brisk walk and noticeably accelerates the heart rate (HR), while vigorous-intensity activity is exemplified by jogging, and causes rapid breathing and a substantial increase in HR. In addition, every adult was urged to perform activities that maintain or increase muscular strength and endurance a minimum of two days each week. It was finally added that because of the dose-response relation between physical activity and health, persons who wish to further improve their personal fitness, reduce their risk for chronic diseases and disabilities or prevent unhealthy weight gain may benefit by exceeding the minimum recommended amounts of physical activity.

The latest updated activity intervention strategies for weight loss and prevention of weight (re)gain in adults were described in ACSM Position Stand by Donnelly et al., (2009). This document clearly recognised physical activity as an important component of weight management. After revising a decade of evidence it was concluded that moderate- intensity physical activity between 150 and 250 minutes per week and energy cost of approximately 1200 to 2000 kcal (~ 5- 8.4 MJ) is effective to prevent weight gain more than 3% in most adults and may result in modest weight loss, however, it was made clear that exercise will only induce modest weight loss when not followed by moderate diet restriction. It was agreed that for greater and clinically significant weight loss, exercise of more than 250 minutes or 2000 kcal (~ 8.4 MJ) per week is needed. It was also indicated after careful investigation of existing evidence, that weight maintenance after weight loss is improved with physical activity of more than 250

minutes per week, although lack of available literature made it hard to conclude on the effectiveness of physical activity programmes for the prevention of weight regain. Apart from that, it was recognised that endurance and resistance training are associated with reduction of risk factors for chronic disease.

The general consensus currently adopts the notion that as little as 30 minutes of physical activity on five days of the week (approximately 2.5 hours per week) can improve health and definitely is a good starting point for previously sedentary individuals (Haskell et al., 2007). However, for people who currently undertake 30 minutes of physical activity it is recommended to try to build up to 60 minutes or more in order to get additional health benefits or minimise the likelihood of further or future weight gain (Donnelly et al., 2009; Blair and Church, 2004). However, despite recommendations, non-compliance to physical activity prescribed messages is quite common and presents a unique challenge to exercise experts and participants. In 2004 it was estimated that 24% American men and 38% of American women were trying to lose weight, however among the many weight loss strategies undertaken, only a third of those surveyed reported eating fewer calories and exercising more (Kruger et al., 2004). In US between 2000 and 2005, the percentages of adults who walked during their usual daily activity, lifted heavy loads during their usual daily activity, and engaged in regular leisure-time physical activity decreased (CDC, 2008; Barnes, 2007). In addition, althought it is known that cardiorespiratory fitness attenuates metabolic risk independently of BMI, the prevalence of meeting the fit but fat definition among US adults is currently 8.9% (Duncan, 2010). On the contrary, physical activity in England has a slightly increasing

trend among both men and women since 1997, with 26% of women and 35% of men in 2004 and 28% of women and 40% of men in 2006 meeting the recommended levels of at least 30 minutes of moderate-intensity activity 5 times a week (NHS, 2008). It is interesting, though, that one in six individuals does not record any moderate physical activity at all (Swan, 2004) and any modest increase has done little to change the high percentage of obesity, with public health messages hardly reach at-risk populations such as women, older adults and those of low social-economic class, or are not having the desired effects when received (Craig et al., 2004).

Although, physical activity recommendations are formed with the ultimate purpose to shed light and present information in a way that leads to the adoption and maintenance of physically active lifestyles, individuals and professionals often face difficulty in translating the public health recommendations. Thompson et al., 2009 showed that some of the most commonly used physical activity recommendations, are confusing either because they use different outcomes (e.g. time component of EE) or sometimes they are very imprecise and even contradictory. Thus physical activity status should be assessed with caution because even ostensibly small differences between recommendations may result in huge status misclassification of the individual. At least the most recent physical activity recommendations managed to clarify some previous inconsistencies, however, it is important to note that possible compensatory responses to exercise regimes are not fully acknowledged (i.e. increased energy intake or decreased spontaneous activity), and reports do not draw attention to the individual, although there are data to suggest individual response (Donnelly et al., 2003; Lamarche et al., 1992). Attention should also

be drawn to the frequency and quantity of exercise and how exercise patterns of different features can be integrated into someones lifestyle to augment both weight regulation and health benefits acquisition. Ways to increase participation and adherence to physical activity should also be investigated.

1.4 Physical activity and energy balance

Exercise interventions divided in short- (single session), medium- (2 days to 4 weeks) and long-term exercise trials (>1 month) for purposes of convenience in this review, attempt to elucidate responses to energy balance perturbations induced by ExEE. According to Blundell and King (1999), when the relationship between exercise and energy intake is examined, four major possibilities can occur:

1) No change in energy intake in response to increased EE - apparently creating a negative energy balance status.
2) A compensatory effect in energy intake in response to increased EE - leading to positive energy balance.
3) An exercise-induced suppression of energy intake in response to increased EE - leading to negative energy balance.
4) Food and/ or nutrient selection changes in response to increased EE - leading to either negative or positive energy balance.

1.4.1 Effect of a single exercise session on appetite and energy intake

Studies investigating the effect of a single exercise session on appetite, and energy intake are presented in Evidence Table 1. To identify the articles included in Evidence Table 1, search engines of the databases MEDLINE and OVID were used for papers published from 1988 to 2010 in English using the terms “exercise”, “acute exercise”, “single exercise” together with “energy intake”, “*ad libitum* food intake”, “buffet meals”, “appetite”. The reference lists of articles retrieved were also examined. Papers were excluded if energy intake was not measured *ad libitum*.

Short-term intervention studies consist of a single bout of exercise with subsequent measurement of energy intake from *ad libitum* meals accompanied sometimes by subjective measurements of appetite sensations and measurements of appetite related hormones. Such studies provide useful insight as to the immediate effects of exercise and possible mechanisms through which these effects are mediated.

The vast majority of evidence obtained from those short-term studies show that a single bout of exercise does not have an impact on subsequent energy intake (King et al., 2010a; King et al., 2010b; Finlayson et al., 2009; Schneider et al., 2008; Erdmann et al., 2007; Maraki et al., 2005; George et al., 2003; Tsofliou et al., 2003; Hubert et al., 1998; Lluch et al., 1998; King et al., 1997; Imbeault et al., 1997; King et al., 1996; King and Blundell, 1995; King et al., 1994; Kissileff et al., 1990; Thompson et al., 1988; Reger et al., 1984) and therefore suggests that coupling between energy intake and energy expended through exercise is weak. Such a result was consistent across lean males (King et al., 2010a; King et al., 2010b; Imbeault et al., 1997; Thompson et al., 1988), lean

(Finlayson et al., 2009; Maraki et al., 2005; George et al., 2003; Hubert et al., 1998; Lluch et al., 1998; Kissileff et al., 1990), overweight (George et al., 2003) and obese females (Tsofliou et al., 2003; Kissileff et al., 1990), across a wide age range of 18-70 years, in different types of exercise including walking (King et al., 2010a; George et al., 2003; Tsofliou et al., 2003), running (King et al., 2010b; Imbeault et al., 1997), cycling (Finlayson et al., 2009; Hubert et al., 1998; Lluch et al., 1998; Kissileff et al., 1990; Thompson et al., 1988), and an aerobic/muscle conditioning exercise class (Maraki et al., 2005), at both low (Imbeault et al., 1997) and high (Hubert et al., 1998; Imbeault et al., 1997; Kissileff et al., 1990; Thompson et al., 1988) intensities. Due to the ExEE of between 120-490 kcal with no impact on energy intake, it is suggested that participants entered negative energy balance (assuming energy balance upon entry to the study). Such an observation is consistent with the reduced estimated relative energy intake [REI (energy intake minus net energy cost of exercise)] calculated in some of those studies (King et al., 2010a; King et al., 2010b; Maraki et al., 2005; Lluch et al. 1998; King et al., 1994).

Some of the studies that found no differences in energy intake compared to the controls assessed in parallel the effects of exercise on appetite sensations. Hunger or "the drive to obtain food" was the primary appetite signal measured, and in addition sensations such as satiety, fullness, desire to eat (DTE) and prospective food consumption (PFC) were assessed. Some of those studies demonstrated a relationship between appetite and energy intake responses (King et al., 2010a; King et al., 2010b; Hubert et al., 1998; Lluch et al., 1998; Imbeault et al., 1997; King et al., 1996; Kissileff et al., 1990) implying no effect

of exercise on subsequent appetite and energy intake. Such a result was found in moderately active young lean males and females in different types of exercise including running (Imbeault et al., 1997), cycling (Hubert et al., 1998) and brisk walking (King et al., 2009) and at both low (Imbeault et al., 1997) and high (Hubert et al., 1998) intensity. However, not the whole body of research, which showed no impact of exercise on subsequent energy intake, shared the same finding. For example, following a single exercise session, obese women (Tsofliou et al., 2003) and lean men after moderate (King et al., 1997), or high intensity exercise (Thompson et al., 1988) and after resistance or aerobic exercise (Broom et al., 2009) felt less hungry than in rest conditions, while Maraki et al., (2005) and Lluch et al., (1998) found lean women to increase appetite. In opposition, Kissileff et al., (1990) showed that exercise has no impact on appetite signals in lean females but found hunger to increase in obese women after moderate intensity physical activity; however this effect was again not translated in greater food intake. As appetite findings are only important when they can be translated to subsequent energy intake, it could be inferred that appetite sensations produced after a single exercise session, may not be related to the subsequent energy intake in the post-trial meal, suggesting differential mechanisms controlling energy intake in addition to perceptions of appetite.

On the other hand there is evidence to suggest that energy intake increased after exercise and this finding was observed in both lean men and women with no accompanying increases in appetite sensations (Finlayson et al., 2009; Martins et al., 2007a; Pomerlau et al., 2004; Lluch et al., 2000; Klausen et al., 1999; Lluch et al., 1998; Verger et al.,

1994; Tremblay et al., 1994). However, there are studies to suggest that the observed increase in energy intake after exercise was combined with imposed high-fat diet (Lluch et al., 2000; Lluch et al., 1998; King et al., 1996; King and Blundell, 1995; Tremblay et al., 1994). Lluch et al., (2000) claimed that offering fatty meals increased energy intake and relative energy intake irrespective of exercise, while Lluch et al., (1998) showed that energy intake increased after a high-fat *ad libitum* meal but relative energy intake decreased. Similarly, evidence that eating high fat foods can prevent exercise inducing any short-term negative energy balance and encourage full or partial compensation in both genders, are drawn from another three studies although relative energy intake was not measured (King et al., 1996; King et al., 1995; Tremblay et al., 1994).

One study concluded that energy intake was significantly higher after exercise trials compared to habitual diet with no difference between high- and low-intensity groups, thus a greater positive energy balance was observed in the low-intensity group (Klausen et al., 1999). Partial energy intake compensation after exercise was also observed in the literature after ExEE of 800 kcal within 2 hours, which significantly increased the energy intake of 58 lean males by approximately 437 kcal (Verger et al., 1994). The degree of exercise-induced EE in this study was considerably greater, in contrast to other studies that had no effect on energy intake and involved an exercise session of no longer than approximately 72 minutes, with ExEE of 120-490 kcal. In a similar way, Pomerlau et al., (2004) indicated almost complete energy intake compensation in the absence of accompanying appetite changes one day after a high-intensity running session of 1 hour

in lean women, in contrast to unchanged energy intake after undertaking low-intensity exercise of the same ExEE.

The notion that physical activity can suppress energy intake, creating in that way negative energy balance, is rarely encountered in the literature (Ueda et al., 2009a; Ueda et al., 2009b; Westerterp-Plantenga et al., 1997). However, this finding is not always accompanied by a similar suppression in subjective appetite measures. One study in particular, found that moderate cycling of 1 hour exerted significantly higher energy intake suppression in obese rather than lean men but appetite did not change in either group (Ueda et al., 2009a). Interestingly, a brief suppression of hunger and energy intake immediately after high-intensity exercise has been observed in several studies in both lean and obese subjects (King et al., 2010b; Ueda et al., 2009b; Westerterp-Plantenga et al., 1997; King et al., 1995; King et al., 1994; Thompson et al., 1994; Kissileff et al., 1990; Reger et al., 1984) and has been termed "exercise-induced anorexia" (Blundell et al., 2003). For example, Thompson et al., (1988) showed that high-intensity cycling of 65% $\dot{V}O_{2max}$ carried out for 29 minutes suppressed the feeling of hunger below that experienced after low-intensity cycling carried out at 35% $\dot{V}O_{2max}$ for 58 minutes, inducing equal EE of approximately 311 kcal. Although the feeling of hunger appeared to be lower for 50 minutes post-exercise (at which point a meal was provided), it was only significant for the first five minutes. Both trials within this study were carried out by lean men and were identical apart from the intensity, suggesting that the short-term suppression of hunger might be related to intensity of exercise as opposed to the ExEE. Again, when King and colleagues (1994) compared low-intensity with high-intensity

and short-duration with long-duration/ high intensity exercise sessions, found hunger to decrease briefly after the two sessions involving high-intensity exercise.

A few speculations have been made about the mechanisms for exercise-induced anorexia. It is possible that a higher intensity exercise causes an increase in blood flow to the muscles in response to higher requirements for oxygen and glucose for energy metabolism, and consequently diverts blood flow away from the gastro-intestinal tract (Westerterp-Plantenga et al., 1997). Other possibilities might be the increased activity of sympathetic nervous system during exercise and the subsequent reduced motility of the gastrointestinal tract, or metabolism associated changes such as blood glucose, insulin and free fatty acid level changes (Westerterp-Plantenga et al., 1997). It has also been related to the greater availability of body reserves due to changes of circulatory conditions (Mayers et al., 1954), such as high plasma lactate levels, elevation of body temperature and appetite hormones involvement (King et al., 1997).

Imbeault et al., (1998) carried out a study involving running, as opposed to cycling (Thompson et al., 1988), and found no effect of high-intensity exercise trials on appetite compared with low intensity trials of equal EE. It is not clear as to why contradictory results are obtained in these studies as both involved healthy lean men of a similar bodyweight and age, as well as a similar fitness and activity levels. One reason of differing results might be that subjects in the study by Imbeault et al., (1998) performed higher intensity exercise at 72% maximum oxygen uptake ($\dot{V}O_{2max}$) as opposed to 65% $\dot{V}O_{2max}$ in the study by Thompson et al., (1998) with a slightly higher ExEE by 171 kcal which may have had an effect, but in theory, a more intensive exercise session should

have induced a greater suppression of appetite. As the results from different studies conflict, this suggests that other factors than intensity may be involved in appetite regulation. Another possibility is that the type of exercise is responsible for differences found among studies. However, King et al., (1995) comparing cycling and running exercise, found that both types of exercise had no significant effect on the total amount of food eaten or the appetite sensations.

Although acute intervention studies allow examination of adaptive changes in energy balance after exercise, their applicability is limited. It should be recognised that internal energy homeostasis is regulated on a long-term basis, allowing daily fluctuations, and therefore such short-term exercise programmes may be insufficient in terms of the energy deficit created to elicit a true compensatory response and/or the duration after the exercise intervention is not long enough in order to track compensatory responses. A few studies (Edholm et al., 1955; Saris et al., 1997) suggested that there is a 2-day lag between exercise-induced EE and energy intake. However, these findings have been subject to criticism and further studies have failed to replicate the same relationship (Edholm, 1977; De Castro, 1997). To overcome this limitation, the duration of the post-exercise observation was prolonged up to 3 days. For example, King et al., (1997) examined the effect of high doses of exercise on energy intake in the 2 days following the exercise session. Results suggested that there was no change in appetite sensations and no compensation in food intake within 48 hours compared with days of no exercise and appetite sensations did not change following exercise. This might suggest that even this prolonged duration is not enough to track compensatory changes found in longer

term exercise interventions (King et al., 2008; Barwell et al., 2008). Blundell et al., 2003 suggested that coupling of EE to energy intake may be loose in the short-term but subsequently energy intake increases and partial compensation occurs up to 16 days after the intervention. However, such suggestions are difficult to verify due to the limited evidence from well-controlled studies that track energy intake with more than one *ad libitum* meal after trial in different polulations.

Most of the short-term studies agree that exercise has no impact on subsequent energy intake, but consensus among the diverse literature is hard to be reached. Due to the many potential confounding factors and study designs involving various types of exercise and the use of different intensity, duration and exercise-induced EE (Kesaniemi et al., 2001), with participants of different age, gender, body composition and fitness level, it is difficult to make fair comparisons between studies to determine why such contentious results were obtained, and whether it is due to differences in exercise protocols or subject-specific characteristics. Despite the varying responses in appetite after exercise, there is no convincing evidence to show a relationship between appetite sensations and subsequent energy intake in the post-trial meal or for the following 24 hours. There is also limited reliable evidence to suggest that exercise-induced EE affected energy intake following exercise up to three days, with the majority of studies consistently showing no impact. It should be noted, however, that many of the exercise sessions induced relatively low energy deficit to the participants, which may have been inadequate to induce a compensatory response. In this context, it would of particular interest to see

how acute exercise of EE close to that recommended for weight loss and prevention of weight gain would affect appetite and energy intake.

Moreover, as results obtained are considerably contradictory, it is suggested that the response of appetite and food intake may incorporate a variety of factors that are specific to the individual. An interesting finding was that of Finlayson and colleagues (2009), who found no effect of a 50-minute cycling session in subsequent energy intake and appetite in the group as a whole in the post-trial meal or for the following monitored time. However, after a closer look “compensators” and “noncompensators” were identified. Compensators increased their food intake, rated the food to be more palatable and demonstrated enhanced implicit wanting for food, while noncompensators ate same amount of or less food after exercise than after rest. As such, it was suggested, that some individuals could be resistant to the beneficial effects of exercise and individuality should be primarily considered in that type of research (Finlayson et al., 2009). Individual response approached differently, suggested that those individuals with lower respiratory quotient (RQ) had a greater ExEE and a lesser increase in energy intake after exercise than those with higher RQ, resulting in a state of negative energy balance (Almeras et al., 1995). Therefore, this evidence suggests that considering groups as a whole might be misleading and hide the true response of each individual.

An advantage of acute studies lies on the fact that accurate measurements of energy intake can be obtained as participants stay in the lab for most of the duration of the experiment. Under laboratory conditions researchers are able to covertly measure food

and fluid intake, whereas in self monitoring techniques of food intake participant's reliability is vital to the outcome. However, coherent limitations can change behaviour of participants towards food in controlled conditions. Laboratory environment, personal and situational norms related to food cues, such as portion size, social influence and food availability are few of the factors that may alter energy intake of participants (Herman and Polivy, 2005; 2008). There is also evidence implying that equally important in subsequent energy intake may be the prior quantity of food ingested (Martins et al., 2007b; Hubert et al., 1998) or the dietary restraint scores of the individuals (Lluch et al., 2000). Most importantly however, this type of study does not allow tracking of body composition and EE components changes, because of the short term observatory duration.

Results from short-term interventions provide useful insight as to the immediate effects of exercise and possible mechanisms through which these effects are mediated, but their use is limited as they cannot be applied to "real-life" longer term exercise programmes. The presence and nature of compensatory mechanisms cannot be ruled out based on evidence from short term studies alone, but medium and long term intervention studies should be employed to better understand behavioural compensatory responses to exercise.

In Table 1, twenty eight acute studies are presented of which:

- seventeen suggest that exercise does not have an impact on subsequent energy intake and seven out of seventeen demonstrated no impact of exercise on appetite measurements.
- eight suggest that energy intake increased after exercise with no accompanying increase in appetite sensations, while five of those studies showed that the increase in energy intake was combined with imposed high-fat diet.
- three show that exercise suppresses energy intake, while a brief suppression of hunger and energy intake after high-intensity exercise is encountered in eight out of twenty eight studies.

Evidence Table 1. Studies assessing the effect of a single exercise session on appetite and energy intake

Name	Participants	Duration	Intervention	Main Outcome	Results	Conclusion	Comments
King JA *et al.*, 2010	14 men Healthy Mean age (y): 21.9 ± 0.5 Mean BMI ($kg \cdot m^{-2}$): 23.4 ± 0.6 Mean BF (%): 19.2 ± 1.2 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): 55.9 ± 1.8	Single bout of ex	Cross over design 1. Con (No Ex) 2. Ex (brisk walking for 60 min at 7.0 ± 0.1 $km \cdot hr^{-1}$) Ad libitum meals at: 1.5-2 and 5-5.5 h after trial Follow up time: 7 h	Appetite measurements EI/ REI/ macronutrient intake AG, glucose, insulin, TG	Net ExEE (KJ): 2008 ± 134 <u>Mean EI at ad libitum meals</u> (KJ) <u>Exercise</u> <u>Control</u> EI 9384 ± 659 9212 ± 588 No Ex effect for all appetite measures, EI, macronutrient intake and blood metabolites REI was sig reduced in Ex trial and En deficit in the Ex was 1836 ± 130 KJ	An acute bout of brisk walking inducing a moderate En deficit did not modify appetite, EI, or AG. Findings lend support for a role of brisk walking in weight control.	Subjectively selected walking pace Population used may prevent generalisation to clinical populations
King JA *et al.*, 2010	9 men Healthy Mean age (y): 22.2 ± 0.8 Mean BMI ($kg \cdot m^{-2}$): 23.6 ± 0.4	Single bout of ex	2 x ~24h experimental trials in a cross over design 1. Con (No Ex) 2. Ex (90 min running at 70% VO_2max)	Appetite measurements EI/ REI/ macronutrient intake AG, glucose, insulin, TG	ExEE (KJ): 5324 ± 186 <u>Mean EI at ad libitum meals</u> (KJ) <u>Exercise</u> <u>Control</u> EI 17.606±1252 17.191 ± 1144 No compensatory increase in EI after Ex trial and En deficit in the Ex was	Ex can induce substantial deficits in energy without eliciting compensatory responses in AG, appetite	Population used may prevent generalisation to clinical populations Substantial energy deficit induced

	Mean BF (%): 17.8 ± 1.7 Mean VO_2max (ml·kg^{-1}·min^{-1}): 60.5 ± 1.5		Ad libitum buffet meals at 2.5, 5.5 and 9 h after trial Follow up time: 9 h + next morning samples		4909 KJ Hunger and PFC were sig suppressed during Ex trial at 0.5, 1 and 1.5 h ($p < 0.05$), while fullness and satisfaction were elevated ($p < 0.05$) Suppressed AG during and immediately after ex ($p < 0.001$) Ex transiently suppressed appetite and AG but each remained no different from control values in the hours afterward Insulin, glucose, TG no interaction effect (trial x time) after Bonferroni test	and EI that would render exercise futile in weight management.	
Ueda *et al.*, 2009a	7 O men, 7 L men Healthy, sedentary Mean age (y): 22.9 ± 3.4; 22.4 ± 4.2 respectively Mean BMI (kg·m^{-2}): 30.0 ± 3.1; 22.4 ± 2.4 respectively	Single bout of ex	Cross over design 1. Con (No Ex) 2. Ex (1h moderate intensity cycling at 50% VO_2max) Preceded by set dinner and set breakfast and followed by ad libitum meal (instant pasta of 1.15 kcal/g) 1h	Appetite measurements EI/ REI GLP-1, PYY, AG, glucagon, insulin	<u>Mean EI, REI at ad libitum meal</u> (kcal) <u>Exercise</u> <u>Control</u> EI-L 692.3±106.9 838.2 ± 113.6 REI-L 196.3±108.1 632.4 ± 116.4 EI-O 614.1± 86.9 944.3 ± 176.1 REI-O -92.5±111.7 661.7 ± 153.0 EI/REI after ex were sig lower than those after Con in both groups ($p < 0.001$) EI/REI suppresion after exercise was significantly larger in obese individuals (EI, $p=0.038$; REI, $p=0.021$) Mean PYY and mean glucagon sig	In young, obese adults, a single bout of moderate ex produced sig negative EB compared with their normal weighted counterparts. This difference cannot be explained by sig increases in plasma	Ad libitum test meal composed by one food item which was repeatedly replenished Use of METS to estimate ExEE and intensity set based on age predicted maximum HR Small follow up time

			after trial Follow up time: 1h		increased during ex in both groups ($p < 0.05$) Mean GLP-1 sig increased during and post ex in both groups ($p < 0.05$) No effect of ex on ghrelin, appetite sensations	PYY and GLP-1 during and post ex.	Hematocrit/ hemoglobin measured Subjects blinded to the purpose of the study Although ExEE was moderate, EI decreased after ex in both groups
Ueda *et al.*, 2009b	10 men Healthy, sedentary Mean age (y): 23.4 ± 4.3 y Mean BMI ($kg \cdot m^{-2}$): 22.5 ± 1.0 Mean VO_2 max ($ml \cdot kg^{-1} \cdot min^{-1}$): 45.9 ± 8.5	Single bout of ex	Cross-over design 1. Con (No Ex) 2. Ex (30 min high intensity cycling at 75% VO_2max) 3. Ex (30 min moderate intensity cycling at 50% VO_2max) Preceded by set dinner and set breakfast and followed by ad libitum meal (instant pasta of 1.15 kcal/g) 30 min after trial	Appetite measurements EI GLP-1, PYY, glucose, insulin	EI sig suppressed after ex in both moderate and high intensity groups compared to rest ($p<0.01$ for both) Hunger sig suppressed during and after ex ($p=0.045$) Mean PYY, GLP-1 sig increased during ex compared to rest ($p<0.001$) Mean PYY sig increased during high intensity ex compared to moderate ($p=0.020$) Mean GLP-1 sig negatively correlated with decreased amount of EI after ex ($p<0.001$) Glucose was suppressed during ex ($p<0.001$) No sig changes in insulin, appetite	In young, healthy males EI sig decreased after moderate and high intensity of ex. Plasma PYY levels rose with increased ex intensity but poorly associated with subsequent EI, while increased plasma GLP-1 levels after ex proportionally suppresses EI	Ad libitum test meal composed by one food item which was repeatedly replenished Small follow up time Hematocrit/ hemoglobin measured Subjects blinded to the purpose of the study Even after moderate ExEE, EI decreased

			Follow up time: 30 min		sensations	after both ex intensities.	
Finlayson *et al.*, 2009	24 women Healthy, non restrained Mean age (y): 24 ± 6.1 Mean BMI ($kg \cdot m^{-2}$): 22.3 ± 2.9	Single bout of ex	Cross over design 1. Con (No Ex) 2. Ex (50 min cycling at ~ 70% HRmax) Preceded by fixed breakfast and followed by ad libitum meal ~ 30 min after trial Follow up time: ~2h	Appetite measurements Explicit liking,implicit wanting and relative preference for the same visual food stimuli EI	ExEE (kcal): 189.3 ± 13.0 Mean EI at ad libitum meal (kcal) Exercise Control EI 1128.2±72.8 1018.1 ± 73.0 No complete EI compensation in the group as a whole However: Noncompensators (NC, n=11) ate same or less amount of food after ex compensators (C, n=11) increased EI after ex No differences between NC and C for characteristics, EE and appetite sesnsations or explicit liking in either trial C rated the test meal as significantly less pleasant ($p<0.05$) after C on compared to NC For implicit wanting C RT decreased sig after ex relative to NC, while NC RT sig increased after the test meal relative to C. Post-hoc analysis revealed that C RT was slower for low fat stimuli at baseline while their RT after the test meal was faster for high fat stimuli	Ex-induced changes in the hedonic response to food could be important in the efficacy of using ex as a means to lose weight. Some individuals could be resistant to the beneficial effects of ex due to a predisposition to compensate for ExEE as a result of implicit changes in food preferences.	Individual compensatory differences may exist after a single bout of ex

					C showed a higher preference for high-fat sweet foods (mean=45.61, SD=15.90) compared to NC (mean=37.93, SD=13.60) independent of trial		
Schneider *et al.*, 2008	65 O men and women 66.2% women Healthy Mean age (y): 34.4 ± 10.7 Mean BMI ($kg \cdot m^{-2}$): 33.5 ± 5.5	Short single bout of ex	A repeated measures design in counterbalanced order 1. Con (3 min of sedentary activity) 2. Ex (3 min of exercise and during one session) Snack foods were presented 10 min after each activity	Mood EI	Mixed-effects regression modeling revealed no significant effect of Ex versus Con condition on EI However, moderational analyses revealed that change in negative mood interacted with condition to predict EI, such that participants who reported increased negative mood during exercise consumed more calories in the Ex compared to the Con condition	A short bout of exercise resulted in mood deterioration and increased EI for some overweight, sedentary individuals.	Restricted food variability in buffet Multi- ethnic population Very short ex duration/ activities Gender may affected findings
Erdmann et al., 2007	A. 2 men, 5 women B. 4 men, 3 women Mean age (y): A. 24.4 ± 0.6 B. 24.8 ± 0.7 Mean BMI ($kg \cdot m^{-2}$): A. 21.4 ± 0.8 B. 22.1 ± 0.8	Single bout of ex	2 groups in cross over design Group A 1. Con (No Ex) 2. LI-Ex (30min at 50 W) EE: 85.6 kcal 3. HI-Ex (30min at 100	Appetite measurements EI AG, Gh, glucose, insulin, glucerol, epinephrine, norepinephrine	In A: Gh increased in LI-Ex but not in HI-Ex Respective appetite ratings and subsequent food intake and postprandial Gh suppression were identical and not different from controls In B:	The present data suggest that LI than HI ex stimulates Gh levels independently of ex duration. Stimulation of food intake	Restricted food variability in buffet Gender may affected findings Small follow up time

			W) EE: 171.2 kcal Group B 1. Con (No Ex) 2. Ex (30, 60, 120 min at 50W) EE: 85.6, 171.2, 342.4 kcal Ex: cycling Preceded by 2 wk wt maintaining diet and followed by ad libitum sandwich meal 15 min after trial Follow up time: A: 105min B: 120 min		Gh rose significantly by 50–70 pg/ml above baseline for the respective period of ex While post ex premeal Gh levels were not significantly different subsequent food intake after 120 min of cycling was significantly greater compared to control, 30 min and 60 min ex, respectively. Appetite was did not change in ex No differences in the rest metabolites in the postprandial period apart from reduction in glycerol in ex	during prolonged ex is most likely not due to changes of Gh.	
Martins *et al.*, 2007a	6 men, 6 women Healthy, sedentary Mean age (y): 25.9 ± 4.6 Mean BMI ($kg \cdot m^{-2}$): 22 ± 3.2	Single bout of ex	Cross over design 1. Con (No Ex) 2. Ex (1h moderate intensity cycling at 65% predicted VO_2max)	Appetite measurements EI/ REI/ macronutrient intake AG, PYY, GLP-1, PP	<u>Mean EE and EI, REI at ad libitum meal</u> (kcal) <u>Exercise</u> <u>Control</u> EI 913 ± 363 762 ± 252 REI 421 ± 302 565 ± 226 EE 492 ± 92 197 ± 37 EI at buffet sig increased and REI at buffet sig decreased in ex trial ($p < 0.05$)	Increased EI in ex trial ad libitum meal was not explained by differences in hunger sensation or changes in appetite	Gender may affected findings Female menstrual cycle not accounted for changes in appetite Use of METS to

	Mean restraint/external/ emotional eating: 2.4 ± 0.6/ 2.7 ± 0.6/ 2.2 ± 0.6		Preceded by set dinner + breakfast and followed by ad libitum buffet meal 1h after trial Follow up time: 1h		Mean PYY, GLP-1, PP sig increased during ex and post ex (p=0.038, 0.011 and 0.001 respectively) Hunger sig increased during ex (p=0.004) but not post ex No effect on AG, rest appetite measurements and macronutrient intake	related hormones. Acute ex is able to reduce REI and induce short term negative EB. Ex induced anorexia may be linked to increased anorexigenic hormones during and after ex.	estimate ExEE and intensity set based on age predicted maximum HR Small follow up time Hematocrit/ hemoglobin measured
Maraki *et al.*, 2005	12 women Healthy, not regular exercisers Mean age (y): 28 ± 6.4 Mean BMI ($kg \cdot m^{-2}$): 21.3 ± 1.6 Mean BF (%): 26.8 ± 3.3	Single bout of ex	Cross-over design (2 x 2 repeated measures) 1. Morning Con (No Ex) 2. Evening Con (No Ex) 3. Morning Ex 4. Evening Ex Ex: 1h moderate intensity aerobic and	Appetite measurements EI/ REI for post trial meal and whole day Mood	Mean ExEE (Kcal): 294 ± 25 Mean Con EE: 55 ± 5 <u>Mean EI</u> (kcal) — <u>Whole day</u> — <u>Post trial</u> Morn-Con — 1656 ± 526 — 482 ± 192 Morn-Ex — 1649 ± 517 — 418 ± 179 Eve-Con — 1843 ± 802 — 654 ± 460 Eve-Ex — 1943 ± 580 — 520 ± 253 No sig difference in PT EI or daily EI between trials <u>Mean REI</u> (kcal) — <u>Whole day</u> — <u>Post trial</u> Morn-Con — 1600 ± 527 — 426 ± 192 Morn-Ex — 1355 ± 519 — 125 ± 181 Eve-Con — 1787 ± 799 — 598 ± 459 Eve-Ex — 1648 ± 572 — 225 ± 265 REI sig lower in Morn-Ex than	Ex increased feelings of appetite including increasing hunger and decreasing satiety but had no sig impact on daily EI. However, REI of the post-trial meal was sig lower in the ex trials compared to controls which may induce a state	Subjects consumed light non- standardised breakfast prior trial EI measured by self recorded 24 h diet record Subjects aware of food intake due to self-recording and therefore may alter normal eating habits Time of first post trial meal

			muscle conditioning exercise class Ad libitum feeding, free living for 24h		Morn-Con for lunch meal (p=0.001) and for whole day (p=0.007). REI sig lower in Eve-Ex than Eve-Con for evening meal (p=0.045) Both morning and evening Ex trials sig increased hunger (p=0.008, p=0.004 respectively) PFC (p=0.019, p=0.016), and decreased satiety (p=0.015, p=0.004) and fullness (p=0.012, p=0.008) post-trial compared to pre-trial Sig higher hunger (p=0.034), PFC (p=0.041), and sig lower satiety (p=0.012) post-trial in Morn-Ex compared to Morn-Con No sig difference in appetite between Ex trials	of negative EB.	consumption not available
Pomerleau *et al.*, 2004	13 women Healthy, moderately active Mean age (y): 22.2 ± 2.0 Mean BMI ($kg \cdot m^{-2}$): 22.2 ± 2.4 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): 44.0 ± 4.7 Restrained/unrestrained	Single bout of ex	Cross over design 1. Con (No Ex) 2. LI-Ex (64min at 40% VO_2max) 3. HI-Ex (37min at 70% VO_2max) Ex: Walk (treadmill) Preceded by set	Appetite measurements EI/ REI for post trial meal, whole day and 3 days post trial	ExEE (kcal): ~350 <u>Mean EI on post-trial day</u> (kcal) <u>Lunch</u> <u>Dinner</u> <u>Daily</u> Con 751±230 660±199 2285±596 LI-Ex 819±236 671±283 2397±432 HIEx 878±309 649±339 2580±529 EI sig greater at lunch after HI-Ex but not LI-Ex compared to Con (p≤0.02). No sig differences in dinner EI or daily EI between trials <u>Mean EI for 3 days post trial</u> (kcal) <u>EI</u> Con 2210 ± 266	Increasing ex intensity in young women leads to an increase in EI during the meal that follows the ex session. Also, the increase in EI on the day of the HI-Ex bout is sufficient to almost completely	Standardised breakfast consumed prior trial EI measured by investigators for buffet lunch, dinner and snacks, by weighed intake EI for 3 days post-trial self-recorded

	eaters: 5/8		breakfast and followed by ad libitum buffet meal 1h after trial and dinner as well as snacks in the afternoon and evening Follow up time: 3 days by self recorded weighted intake		LI-Ex 2138 ± 500 HI-Ex 2194 ± 428 No sig difference in EI for 3 days post-trial <u>Mean REI</u> (kcal) <u>Lunch</u> <u>Daily</u> Con 751 ± 230 2285 ± 596 LI-Ex 530 ± 233 2108 ± 435 HI-Ex 565 ± 307 2266 ± 528 REI at lunch was sig lower in HI-Ex ($p<0.01$) and LI-Ex ($p<0.001$) compared to Con. No sig difference in lunch REI in HI- and LI-Ex trials. No sig differences in mean daily REI between trials Exercise had no sig effect on appetite ratings	compensate for the ExEE.	Daily EE was not measured No sig difference in EI between restrained and unrestrained eaters across trials A more profound compensation of ExEE occurred after the HI-Ex day (91%) than after the LI-Ex day (40%), but this difference was not significant
George *et al.*, 2003	12 L women 12 OW women Healthy, sedentary Mean age (y): 35 ± 8 Mean BMI ($kg \cdot m^{-2}$): 22 ± 1, 28 ± 1 respectively	Single bout of ex	Cross sectional (2 x 2 repeated measures design) 1.Con (No Ex) 2.Ex (60 min walking at 60% HRmax) Preceded by set breakfast and followed by ad lib feeding 30min post-trial, alone,	EI Macronutrient intake	ExEE:150-200 kcal <u>Mean EI in ad libitum meal</u> (kcal) <u>Ex</u> <u>Con</u> L 359 ± 128 441 ± 229 OW 576 ± 263 525 ± 173 Sig higher EI in the OW women compared to L in both Ex and Con ($p<0.027$) Sig higher % fat intake in the OW women compared to lean in both Ex and Con ($p<0.031$)	OW women ate more than lean in both ex and con trials but there was no sig impact on EI post-Ex within groups of either lean or OW women.	EI measured by weighed intake by investigators Subjects unaware EI was monitored after Ex Large food choice in familiar setting

			from cafeteria Follow up time: 30 min		No sig difference in EI between Con and Ex in either lean or OW women		
Tsofliou *et al.*, 2003	10 obese women Healthy, 5 pre and 5 post-menopausal Mean age (y): 50.0 ± 8.5 Mean BMI ($kg \cdot m^{-2}$): 37.2 ± 6.5 Mean BF (%): 47.4 ± 3.9	Single bout of ex	Cross-over design All subjects watched food related TV for 1 h, then entered 1 of the interventions for 20-30 min 1. Con (no Ex or snack for 30 min) 2. Snack 3. Mod-Ex (20mins brisk walking at 13 of the RPE scale) Preceded by set lunch and followed by ad libitum dinner 1 h post-trial Follow up time: 1 h	Appetite measurements EI Leptin, FFA	ExEE (kcal): 120 Mod-Ex and snack intervention sig increased satiety (p=0.01) and fullness (p=0.02, p=0.01 respectively) compared to control immediately after trial. Satiety remained sig higher 1hr post-Ex trial (p=0.02) Desire to eat and PFC immediately after Ex was sig lower than Con (p=0.03, p=0.009 respectively). Hunger immediately after Ex was not sig different from baseline or Con Hunger increased sig 1hr post-trial in all 3 interventions; Con ($p \leq 0.01$), snack ($p < 0.05$), Mod-Ex ($p < 0.05$) <u>Mean EI at ad libitum meal</u> (kcal) — <u>EI</u> Con — 724 (509 – 1369) Snack — 657 (541 – 742) Mod-Ex — 683 (509 – 1011) No sig difference in EI between trials No sig difference in serum leptin levels between trials. Plasma FFA sig higher after Ex (p=0.009) than Con or Snack. Plasma glucose sig	Ex may prevent or attenuate weight gain and possible negative EB due to lack of EI compensatory effects in obese women.	EI measured by weighed intake by investigators Snack intervention sig suppressed hunger immediately post-trial compared to Con (p=0.01) and Ex (p=0.03)

					higher after snack (p=0.02) than after Ex or Con trials		
Lluch *et al.*, 2000	13 unrestrained women (UN) 12 restrained women (R) Healthy Mean age (y): (UN): 22.6 ± 2.3 (R): 21.7 ± 2.2 Mean BMI ($kg \cdot m^{-2}$): (UN): 21.9 ± 1.6 (R): 22.6 ± 1.9 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): (UN): 37.0 ± 3.3 (R): 41.0 ± 4.4	Single bout of ex	2 x 2 repeated-measures design 1. Con + high-fat ad libitum lunch 2. Con + low-fat ad libitum lunch 3. Ex (70% VO_2 max, 50 min) + high-fat ad libitum lunch 4. Ex (70% VO_2 max, 50 min) exercise session + low-fat ad libitum lunch Preceded by set breakfast and followed by ad libitum test meals immediately after trial	EI, REI Post meal hedonic ratings	EI and REI increased during high-fat conditions compared with the low-fat, independently of ex ($p<0.001$) There was a positive relationship between dietary restraint scores and EI or REI in the con conditions only ($r= 0.54$, $p<0.01$) The decrease of REI between the con and ex conditions was higher in R than in UR ($p<0.01$). There were no relationships between food hedonic ratings and EI, REI for the level of dietary restraint	These results confirm that a high-fat diet reversed the energy deficit due to ex. There was no energy compensation in response to an acute bout of ex during the following meal. In R eaters, ex was more effective in creating an energy deficit than in UR eaters. Ex may help R eaters to maintain control over appetite.	Not long follow up duration
Klausen *et al.*, 1999	16 men, 16 women 16 old, 16 young Healthy, not regular exercisers	Single bout of ex	Randomised cross-over design <u>Day 1</u>: subjects	EI post ex compared to habitual diet Macronutrient	<u>Mean ExEE and daily EE</u> (kcal) <u>ExEE</u> <u>Mean EE/d</u> LI-Ex 179 (158 – 200) 2069 HI-Ex 194 2105	ExEE causes an increase in EI compared to habitual diet with no	Did not include a control Habitual diet determined by 2

	Mean age (y): 50 young approx. 30 old approx. 70 Mean BMI ($kg \cdot m^{-2}$): 22.5 Mean BF (%): 21.6 Mean VO_2max ($l \cdot min^{-1}$): 2.53		ate standardised diet and randomly assigned to 1 of 2 interventions in whole-body calorimeter 1. LI-Ex (cycling 60min at 30% VO_2max) 2. HI-Ex (cycling 30 min at 60% VO_2max) <u>Day 2</u>: In lab, subjects fed ad libitum from buffet at breakfast and lunch and self-recorded food intake for rest of day and during day 3 Follow up time: 3 days	intake Mean daily EE	(167 – 220) Sig higher ExEE and mean EE/d in HI-Ex group ($p<0.01$) <u>Mean EI</u> (kcal/d) — <u>EI</u> Habitual Diet — 2229 (2005 – 2453) Following LI-Ex — 2564 (2294 – 2834) Following HI-Ex — 2615 (2355 – 2875) Sig higher EI day after both HI-Ex and LI-Ex compared to habitual diet ($p<0.01$) No sig difference in EI between LI-Ex and HI-Ex ($p<0.05$). <u>EB (kcal/d)</u> LI-Ex: 95 (36-155) HI-Ex: 59 (1-116) ($p<0.01$)	sig difference between HI and LI Ex. This resulted in a positive EB to a greater extent with LI-Ex.	day weighed intake – may not be fully representative EI weighed and recorded by investigators on day 2. EI self-recorded on day 3 Large range of EI. No separate data for males and females Sig 4.2% greater fat intake day after HI-Ex ($p<0.01$) and 3.2%greater fat intake after LI-Ex ($p<0.05$) compared to habitual diet. % CHO intake was therefore sig lower following Ex compared to habitual diet Limited data with regards to gender and age-group differences

Almeras *et al.*, 1999	11 men Healthy, sedentary to moderately active Mean age (y): 30 Mean BMI ($kg \cdot m^{-2}$): 24.5 Mean BF (%): 19.2 ± 8.9 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): 42.0 ± 8.4	Single bout of ex	Cross over design <u>Day 0</u>: randomly assigned to 1 of 2 interventions: 1. Con (No Ex) 2. Ex (cycling for 90min at 60% VO_2max) Post-trial, Con given dinner of 597 kcal. Ex given same meal but allowed to consume more. <u>Day 1 + 2</u>: Ad lib feeding (2 day EI effect)	Ex RQ EI	<u>RQ during Ex:</u> High RQ: 0.93 (n=5) Low RQ: 0.91 (n=6) Sig different RQ between the two groups ($p \leq 0.01$) <u>Mean ExEE (kcal):</u> High RQ: 716 (597 to 812) Low RQ: 931 (812 to 1170) Sig greater ExEE occurred in the low RQ group compared to subjects with high RQ ($p<0.05$) <u>Mean total EI</u> <u>(kcal)</u> <u>Total EI</u> Con 7284± 1194 Ex 7953± 1242 HighRQCon 6998± 1337 High RQ Ex 8001± 1480 LowRQCon 7499± 1170 Low RQ Ex 7905± 1146 No sig difference in EI between Ex and Con No sig difference in EI between Low RQ and High RQ subjects in Con or Ex Low RQ subjects had negative EB (-406 kcal) and High RQ subjects had postive EB (+406 kcal). The difference was sig ($p<0.05$)	ExEE had no effect on EI for 2 days post-Ex compared to Con. However, analysing data based on RQ showed subjects with a low RQ had a higher ExEE and a lesser increase in EI after Ex than those with a high RQ resulting in a state of negative EB where as subjects with a high RQ entered positive EB.	EI measured by recorded weighed intake in lab occured in labs as well as snacks provided for outside lab EB measures based on assuming daily EE post-ex were same in both Con and Ex trials Low RQ subjects had sig greater BW (70.3kg vs 79kg) and an increased energy cost of Ex
Hubert *et al.*, 1998	11 women	Single bout of ex	Cross-over design	Appetite measurements	<u>ExEE (kcal):</u> 317 ± 44	ExEE had no impact on	Subjects exercised in

	Healthy, regular exercisers, unrestrained eaters Mean age (y): 23.2 ± 2.7 Mean BMI ($kg \cdot m^{-2}$): 21.5 ± 1.1 Mean BF (%): 22.8 ± 1.7 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): 37.6 ± 3.9		1. Con + HEB 2. Con + LEB 3. Ex + HEB 4. Ex + LEB Ex: 40mins cycling at 70% VO_2max HEB: 500 Kcal LEB: 64 Kcal Trials immediately followed by high or low energy breakfast and by ad libitum meal 4h after Follow up time: 4h	EI	<u>Mean EI</u> (kcal) <u>Breakfast</u> <u>Lunch</u> Ex + HEB 495 ± 36 597 ± 215 Ex + LEB 64 ± 7 679 ± 679 No Ex HEB 500 ± 42 603 ± 196 No Ex LEB 64 ± 7 760 ± 187 No sig effect of ex on EI No sig effect of ex on hunger ratings Sig higher EI in LEB at lunch compared to breakfast and HEB trials ($p<0.05$), but did not fully compensate for LEB Sig higher hunger ratings in LEB trials immediately after lunch and at end of day than HEB	hunger or EI indicating no EI compensatory effect.	fasted state EI recorded by weighed intake in lab
Lluch *et al.*, 1998	12 women Healthy, regular exercisers, restrained eaters Mean age (y): 21.7 ± 2.2 Mean BMI ($kg \cdot m^{-2}$): 22.6 ± 1.9	Single bout of ex	Cross-over design 1. Con + LF 2. Con + HF 3. Ex + LF 4. Ex + HF Ex: 50mins cycling 70% VO_2max	Appetite measurements EI	<u>ExEE (kcal)</u>: ExLF: 425 ± 60 ExHF: 422 ± 59 No sig difference in ExEE between the two Ex trials <u>Mean EI at ad libitum meal</u> (kcal) <u>EI</u> <u>REI</u> Con LF 773 ± 131 722 ± 129 Con HF 1225 ± 236 1175 ± 235 Ex LF 702 ± 140 276 ± 118	Ex increased hunger ratings in the evening but had no sig impact on EI either immediately after Ex or for the rest of the day, and therefore no	Breakfast, lunch dinner recorded by weighed intake by investigators in lab. After dinner snack EI measured by self-recorded intake Food intake

	Mean BF (%): 25.6 ± 2.2 Mean VO_2max (ml·kg^{-1}·min^{-1}): 41.0 ± 4.4		Preceded by set breakfast and followed by ad lib feeding of test meal consisting of either Low Fat or High Fat food 20 mins post exercise. EI monitored for rest of day Follow up time: whole day		Ex HF 1237 ± 273 815 ± 238 No sig difference in total EI between Ex vs no Ex trials. EI increased by 67% in HF trials compared to LF trials ($p<0.001$). REI sig decreased by 43% in Ex trials compared to Con ($p<0.001$). EI and REI of test meal sig increased by 67% and 99% respectively in HF trials compared with LF trials ($p<0.01$) <u>Mean EI for whole day</u> (kcal/d) Total EI Total REI Con LF 2274 ± 433 2224 ± 433 Con HF 2554 ± 548 2504 ± 548 Ex LF 2122 ± 528 1686 ± 504 Ex HF 2566 ± 529 2144 ± 497 No sig difference in total EI between Ex vs no Ex. REI was a sig 19% lower in Ex compared to No Ex ($p<0.01$). Hunger ratings sig lower in Ex trials during 9:00-13:00 ($p=0.56$) and sig higher between 17:00-21:00 ($p=0.01$). However, over the course of whole day, Ex had no sig impact on hunger. (Ex trial took place at 11.50am)	EI compensation occurred. However, consumption of HF, but not LF diet, overcame the ex-induced energy deficit due to energy density as opposed to quantity of food consumed.	restricted between 3 meals. Only 1 drink (including water) was allowed between three meals Although similar amount of food eaten, sig greater EI in HF vs LF test meal due to greater energy density Sig increase in tastiness and pleasantness of LF foods ($p<0.05$) but not HF foods after Ex compared to Con No data for total EE
Westerterp-Plantenga *et al*., 1997	Protocol 1: 10 OW men, 10 L men Protocol 2:	8 times during 8 consecutive weeks on a fixed	Randomised cross-over design Protocol 1:	EI Taste perceptions hedonic rating,	No sig differences between results of OW and L men in all variables <u>Mean EI at ad libitum meals</u>	Ex induced suppression of hunger and a lower EI compared	The EI prior ex was sig lower than rest, possibly in anticipation of

	10 L men Healthy Mean age (y): 25 ± 6; 25 ± 7 respectively Mean BMI (kg·m^{-2}): 28.5 ± 1.9; 22.8 ± 1.6 respectively	d/week	subjects performed ex on four occasions and rest on four occasions Protocol 2: subjects used sauna on four occasions and rest on four occasions Ex: 2h at 60% Wmax cycling Ad libitum feeding from buffet, twice before Ex and 10 mins post-trial. Follow up time: 10 min	appetite sensations, thirst and macronutrient choice	(kcal) Prior trial Post trial Con 740 740 Ex 238 549 EI sig lower both pre and post trial in ex than rest trial ($p<0.001$). EI sig lower post trial in sauna than rest trial ($p<0.01$) Hunger was sig suppressed after ex compared to rest trial ($p<0.01$) Thirst was sig increased after ex compared to rest trial ($p<0.0001$) and after sauna compared to rest trial ($p<0.0001$) Satiety rating was not sig different between trials	with control, consequently subjects entered negative EB reflected in the sig reduction in BW.	exercise – not controlled for Time between EI prior trial and time trial commenced was not stated. % CHO of dietary intake increased and % fat decreased after ex Sig reduction in BW compared to baseline in exercise trial (-1.86 kg), ($p<0.001$) and sauna trial (-1.82 kg), ($p<0.001$)
NA King *et al.*, 1997	8 men Healthy, regular exercisers Mean age (y):26 ± 5.2 Mean BMI (kg·m^{-2}): 22.4 ± 1.8	2 bouts of ex	Cross over design over 2 days 1. Con (Two days of No Ex: R1/R2) 2. Ex [Day 1: 50 min Ex in	Appetite measurements EI EE	ExEE Ex1(kcal): Morning: 581 ± 119 Afternoon: 610 ± 122 Mean total EI: (kcal) EI R1 2903 ± 546 R2 2903 ± 546	ExEE suppressed same day hunger compared to the following day, but did not affect EI leading to a	EI measured through self recorded weighed intake – data was consistent with predicted data indicating under-reporting unlikely

			the morning + 50 min Ex in afternoon (Ex1), Day 2: No Ex (Ex2)] Ex: Running at 70% VO_2max Ad lib feeding of habitual diet for 2 days post-trial Follow up time: 2 days		Ex1 2981± 498 Ex2 2726 ± 538 No sig difference in EI between days or between trials No sig difference in EE (excluding ExEE in Ex1) Hunger on Ex1 was lower than R1 and R2, but not sig different. Hunger on Ex1 was sig lower than Ex2 ($p<0.05$)	state of negative EB due to largeExEE.	Standardised breakfast consumed prior trial Free living - time of eating not constant between subjects Due to large energy deficit may see EI compensation over a longer observation period than 2 days
Imbeault *et al.*, 1997	11 men Healthy, moderately active Mean age (y): 24.4 ± 3.3 Mean BMI ($kg \cdot m^{-2}$): 23.2 ± 2.3 Mean BF (%): 11.8 ± 6.0 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): 56.7 ± 5.0	Single bout of ex	Cross over design 1. Con (No Ex) 2. LI-Ex (running 72 min at 35% VO_2max) 3. HI-Ex (running 34 min at 72% VO_2max) Preceded by set breakfast and followed by ad	EI (Kcal) REI (Kcal) Appetite (hunger, fullness)	ExEE (kcal): LI: 490 ± 10 HI: 482 ± 9 No sig difference in ExEE between Ex-trials. Approx. mean EI/REI at ad libitum meal (kcal) EI REI Con 1580 1580 LI-Ex 1770 1370 HI-Ex 1585 1150 No sig difference in EI between trials. Sig lower REI after HI-Ex	Ex had no impact on appetite or EI. However, HI-Ex, but not LI-Ex sig reduced REI compared to Con, therefore inducing a state of negative EB.	Approx 40 food choices from buffet EI measured through weighed intake by investigators REI did not account for resting EE

			libitum buffet, 15 min after trial		compared to LI-Ex ($p<0.05$) and control ($p<0.001$). No sig difference in hunger and fullness ratings between trials.		
King NA *et al.*, 1996	13 women Unrestrained Lean, healthy	Single bout of ex	2 x 2 repeated measures design in a counterbalanced order 1. Con + high-fat/low-CHO free selection test lunch 2. Con + low-fat/high-CHO free selection test lunch 3. Ex (70% VO_2 max) + high-fat/low-CHO free selection test lunch 4. Ex (70% VO_2 max) + low-fat/high-CHO free selection test lunch	Appetite measurements EI/ macronutrient intake	Ex did not suppress hunger Women rated a range of foods to be more palatable after ex ($p< 0.05$) Similar to male subjects, ex in females had no sig short-term effect on EI or macronutrient intake. EI was sig influenced by fat. CHO composition of the foods available ($p< 0.001$), and the short-term energy deficit induced by ex when followed by low-fat lunch was completely wiped out when exercise was followed by a high-fat lunch ($p< 0.001$)	Consumption of HF, but not LF diet, overcame the ExEE due to energy density as opposed to quantity of food consumed.	Comparison with study on men
King NA *et al.*, 1995	24 men Lean, healthy	Single bout of ex	2 studies [cycling (CYC) and running (RUN)], 2x2 design, with 4	Appetite measurements EI/ macronutrient	CYC and RUN produced similar effects on appetite responses CYC and RUN induced a transitory suppression of hunger ($p< 0.01$ and	These results indicate that eating high-fat foods can prevent Ex	For the remainder of the day (outside of laboratory) was monitored by

			treatments each: 1. Con + high-fat/low-CHO free selection test lunch 2. Con + low-fat/high-CHO free selection test lunch 3. Ex (70% VO2 max) + high-fat/low-CHO free selection test lunch 4. Ex (70% VO2 max) + low-fat/high-CHO free selection test lunch Follow up time: whole day	intake	p< 0.05) and a delay to the onset of eating (p< 0.001) CYC or RUN had no sig effect on the total amount of food eaten, but there was a sig effect of lunch type. When provided with the high-fat/low-CHO foods EI was sig elevated (CYC: p < 0.001; and RUN: p < 0.0001). Both types of exercise induced a short-term negative EB when followed by the low-fat/high-CHO foods (p < 0.001), which was completely reversed (positive energy balance) when subjects ate from the high-fat/low-CHO foods	inducing any (short-term) negative EB. Therefore, in order for Ex to have a sig impact on weight control, it is important to consider the energy density of the accompanying diet. CYC and RUN did not display different effects on appetite.	providing the subjects with airline-style food boxes Comparison with study on women
Verger et al., 1994	58 men Healthy, physically active Mean age (y): 18-22 Mean BMI ($kg \cdot m^{-2}$): 21.3 ± 1.6	Single bout of ex	Cross over design 1. Con (No Ex) 2. Ex (2h running and jumping cross country) Preceded by	EI	<u>Mean ExEE (kcal):</u> 800 <u>Mean EI (kcal)</u> Con: 1672 ± 110 Ex: 2109 ± 126 Sig greater EI after ex compared to Con (p<0.05)	EI was sig greater after ex than control, but ex induced increase was lower than the EE during ex.	EI measured by weighed intake by investigators. Over 50 food choices from buffet Did not state intensity of

			regular lunch and followed by ad libitum buffet, alone, 30 min after trial Follow up time: 30 min				exercise % EI of protein sig greater post-Ex compared to Con ($p<0.0001$)
Tremblay *et al.*, 1994	9 men Healthy, sedentary-moderately active Mean age (y): 28.3 ± 6.1 Mean BMI ($kg \cdot m^{-2}$): 24.2 Mean BF (%): 14.7 ± 7.7 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): 54.7 ± 6.6	Single bout of ex	Cross over design 1. Con 2. Ex + LF diet 3. Ex + M diet 4. Ex + HF diet Ex: Running for 60 min at 55-60% VO_2max Followed by ad libitum meal to specified diet, for 48h Follow up time: 2 days	EI EB	<u>Mean ExEE in each Ex trial (kcal):</u> 668 ± 95 <u>Mean EE post-trial (kcal)</u> <u>(kcal)</u> <u>Day 1</u> <u>Day 2</u> Con 2627 ± 453 3033 ± 859 Ex+LF 3654 ± 835 3487 ±1194 Ex+M 3296 ± 644 3057 ± 812 Ex+HF 3439 ± 597 3511 ±1003 Sig greater EE on Day 1 in Ex trials compared to Con ($p<0.05$). Sig greater EE in Ex+LF after 48h compared to Con ($p<0.05$) <u>Mean EI (kcal/d)</u> <u>(kcal)</u> <u>Day 1</u> <u>Day 2</u> Con 3343 ± 382 3009 ± 549 Ex+LF 3391 ± 597 2746 ± 310 Ex+M 3152 ± 549 2651 ± 525 Ex+HF 3964 ± 740 3762 ± 668 Sig greater EI in the Ex-HF trial in both day 1, day 2 compared to other three trials ($p<0.05$). No sig difference between Ex+M, Ex+LF and Con. <u>Approx. EB (kcal/48hrs):</u>	Despite a sig increase in EE in all Ex trials due to ExEE in addition to higher daily EE, EI only increased sig in the Ex-HF. As a result the Ex+M and Ex+LF entered negative EB, where as the Ex+HF and the Con entered positive EB. A HF diet therefore compensates for ExEE.	Free living Con had diet composition and activity level representative of lifestyle of free-living population EI measured by recorded weighed intake in lab by investigators. Snacks provided to subjects for outside lab consumption Whether subjects ate a standardised meal prior Ex was not mentioned

					Con: + 700 Ex + LF: -1003 Ex + M : - 370 Ex + HF: + 740 Sig difference in EB between Con and Ex+LF ($p<0.05$). Sig difference in EB between Ex+LF and Ex+HF ($p<0.05$)		
King NA *et al.*, 1994	23 men Lean, healthy	Single bout of ex	Subjects randomly assigned: A.- Con (No Ex) - Ex (LI) - Ex (HI) B.- Con (No Ex) - Ex (short duration) - Ex (long duration / HI) Followed by volitional onset of eating from a free-selection test meal Follow up time: 2 days	Appetite measurements Volitional onset of eating EI/ macronutrient intake	Subjective feelings of hunger were sig suppressed during and after intense ex sessions ($p< 0.01$), but the suppression was short-lived. Ex sessions had no significant effect on the total amount of food consumed in the test meal but intense exercise delayed the start of eating ($p< 0.05$). When EI was assessed relative to the energy expended during the exercise or control periods, only the long duration, high intensity session created a significant short-term negative energy balance ($p< 0.001$).	Results indicate that ex-induced anorexia can be characterized by a brief suppression of hunger, accompanied by a delay to the onset of eating. The temporal aspects of ex-induced anorexia may best be measured by the resistance to begin eating rather than the amount of food consumed.	

Verger *et al.*, 1992	13 men and women Healthy, physically active Mean age (y): 20-25 Mean BMI ($kg \cdot m^{-2}$): women: 19.5 ± 1.7 men: 23.4 ± 1.5	Single bout of ex	Groups of 2 or 3 assigned to five test conditions in a counterbalanced order: 1. Con (No Ex + ad libitum meal 60 min after Ex) 2. Ex [(2h at 70-80% HR max (~500 kcal) + ad libitum meal immediately after Ex] 3. Ex at [2h at 70-80% HR max (~500 kcal) + ad libitum meal 30 min after Ex] 4. Ex [2h at 70-80% HR max (~500 kcal) + ad libitum meal 60 min after Ex] 5. Ex [2h at 70-80% HR max (~500 kcal) + ad libitum meal 2h after Ex]	Appetite measurements EI/ macronutrient intake	<u>Mean ExEE (kcal):</u> ~500 The pre-meal hunger rating was sig increased when the meal was offered 1 h after ex as compared to Con ($p<0.01$). Responses obtained in males and females did not differ sig Mean post-meal hunger ratings were similar between all Ex trials After ex, the later the meal was presented, the larger was the amount consumed: the difference between T0 and T30 did not reach statistical sig, but the increases from 0 to 60 and from 0 to 120 were highly sig, ($p< 0.01$) No difference was observed between Ex and Con in the percentage of calories from the three macronutrients consumed at noon. With delay after ex, caloric intake as protein or as lipid did not change, but the more the meal was delayed, the higher the caloric intake from CHO became, being sig augmented at 60 and 120 relative to 0, ($p\sim0.01$) The percentage of calories consumed as protein decreased from 0 to 30, 60 and 120, respectively, ($p<0.01$), the percentage as CHO increased from 0 to 60 and 120, ($p < 0.05$), while the percentage of calories from lipids did not change	Ex did not induce energy compensation. The percentage of energy as protein chosen in the foods decreased as the delay between the end of Ex and meal presentation increased.	Ad libitum water consumption during trials

			Follow up time: depended on trial		Males and females responded in the same way		
Kissileff *et al.*, 1990	9 L women, 9 OW women Healthy Mean age (y): L: 22.7 ± 4.9 OW: 24.3 ± 4.8 Mean BMI ($kg \cdot m^{-2}$): L: 22.1 ± 1.8 OW: 27.7 ± 0.9 Mean BF (%): L: 27.1 ± 2.8 OW: 38.7 ± 2.7 Mean VO_2max ($L \cdot min^{-1}$): 1.9-3.0	Single bout of ex	Cross-over design 1. Con (No Ex) 2. MI-Ex (cycling for 40min at 30W) 3. HI-Ex (cycling for 40min at 90W) Preceded by set breakfast and followed by ad libitum test meal 15 min post-trial, (yoghurt) Follow up time: 15 min	Appetite measurements EI	<u>Mean ExEE</u> (kcal) Obese Lean Con 35.8 ± 4.9 35.2 ± 6.7 MI-Ex 143.2± 33.3 113.7± 36.7 HI-Ex 237.2± 25.1 246.8± 24.3 No sig differences in ExEE between OW and L <u>Mean EI (test yoghurt)</u> (kcal) Obese Lean Con 658 ± 353 736 ± 316 MI-Ex 605 ± 262 783 ± 261 HI-Ex 552 ± 275 644 ± 339 In L subjects, EI was sig lower after HI-Ex than MI-Ex ($p=0.03$) but neither Ex trial was sig different from Con In OW subjects, no sig difference in EI between Con and Ex trials Hunger was sig higher in OW after MI-Ex compared to HI-Ex or Con ($p<0.05$)	ExEE had no impact on hunger in L but increased in OW after MI-Ex only. This feeling did not translate into EI as there was no sig difference in EI between trials in OW subjects. In contrast, HI but not LI ex resulted in reduced EI 15 min post-trial, in L women.	Subjects unaware EI was being measured Standardised breakfast (300 kcal) consumed 2hrs prior trial Test meal rated slightly-moderately palatable. May have had effects on EI in some subjects Restraint scores similar in OW and L
Thompson *et al.*,1988	15 men Healthy Mean BMI ($kg \cdot m^{-2}$):	Single bout of ex	Cross-over design 1.Con (No Ex) 2.LI-Ex	Appetite measurements EI/ macronutrient	<u>Mean ExEE (kcal):</u> 4.1 kcal/kg BW (approx. 311kcal for both) Hunger ratings in HI-Ex were sig lower than LI-Ex and CON 5min	High intensity, but not low intensity ex, suppresses	Subjects exercised in fasted state EI measured by

	22.1 ± 1.8 Mean age (y): 23.8 ± 3.9 Mean BF (%): 15.6 ± 3.1 Mean VO_2max (ml·kg^{-1}·min^{-1}): 46.6 ± 5.0		(cycling at 35% VO_2max) 3.HI-Ex (cycling at 68% VO_2max) Followed by ad libitum meal for 20 min alone, 50 min after trial Follow up time: 50 min	intake	post-trial ($p<0.01$). Hunger remained lower at 20, 35, 50 min post-trial in HI-Ex but not sig No sig difference in EI between trials EI in liquid form sig higher in Ex than Con ($p<0.05$) CHO intake sig higher in Ex than Con ($p<0.01$)	hunger for a short duration, with no effect on EI 50min post-ex. Due to eucaloric EE in both Ex trials, this indicates intensity of Ex can influence appetite, independently of EE.	weighed intake by investigators. Subjects unaware EI was measured Subjects knew about meal 1h post-ex. May have influenced perceived hunger Limited food choice

Abbreviations. AG, acylated ghrelin; Approx., approximately; BMI, body mass index; BW, body weight; BF, body fat; CHO, carbohydrates; Con, control; EB, energy balance; EE, energy expenditure; EI, energy intake; Eve-Con, evening control; Eve-Ex, evening exercise; Ex, exercise; ExEE, exercise energy expenditure; F, females; FFA, free fatty acids; Gh, ghrelin; GLP-1, glucagon like peptide -1; HEB, high energy breakfast; HI-Ex, high-intensity exercise; HF, high fat; HR, heart rate; L, lean; LEB, low energy breakfast; LI-Ex, low-intensity exercise; LF, low fat; max, maximum; M, males; M, mixed; MET, metabolic equivalent; MI, moderate-intensity; Mod-Ex, moderate exercise; Morn-Con, morning control; Morn-Ex, morning exercise; O, obese; OW, overweight; PFC, prospective food consumption; PP, peptide P; PT, post trial; PYY, peptide YY; REI, relative energy intake (EI minus energy cost of exercise above the resting level); RQ, respiratory quotient; RT, reaction time; Sig, significant; TG, triglycerides; VO_2, oxygen uptake; WC, waist circumference

1.4.2 Effect of medium-term exercise programmes on appetite and energy balance

Studies to investigate the effect of medium-term exercise programmes on energy balance are included in Evidence Table 2. To identify the articles included in Evidence Table 2, search engines of the databases MEDLINE and OVID were used for papers published from 1982 to 2010 in English using the terms “physical activity”, “exercise intervention”, “repeated bouts of exercise”, “medium-term exercise”, “fitness” together with “energy intake”, “*ad libitum* food intake”, “appetite”, “energy expenditure”, “energy balance”. The reference lists of articles retrieved were also examined. Papers were excluded if energy intake and/ or components of total energy expenditure (TEE) were not measured and/or if participants were following specific diets.

Several researchers have carried out studies involving multiple bouts of exercise to investigate whether the greater energy deficit over the medium-term would have an effect on appetite and/or energy compensation. The longer duration of medium-term interventions allows measurement of post exercise energy intake and EE as potential factors of compensation in addition to body composition assessment. There are a few studies assessing the impact of medium-term exercise programmes on appetite and subsequent energy intake lasting for duration of between 5-19 days. The pool of evidence is derived from research conducted on lean (Whybrow et al., 2008; Stubbs et al., 2004a; Stubbs et al., 2004b; Stubbs et al., 2002a; Staten, 1991; Woo and Pi-Sunyer, 1985) or overweight males (Mc Laughlin et al., 2006) and lean (Whybrow et al., 2008; Mc Laughlin et al., 2006; Stubbs et al., 2002b; Staten,1991) or obese females (Woo and Pi-Sunyer, 1982a; Woo and Pi-Sunyer , 1982b), while one study included reduced-obese

females (Keim et al., 1996). Moreover, five studies measured the effects of exercise on appetite in addition to energy intake (Whybrow et al., 2008; Stubbs et al., 2004a,b; Stubbs et al., 2002a,b).

Among these studies there are some to suggest that few days of exercise induce an increase or partial compensation in energy intake and this consequently negates the potential of exercise to produce body mass reduction. For example, partial energy intake compensation in men was observed in the literature after 5 days of exercise, whereas women did not increase their food intake (Staten, 1991). However, the researcher stated that although exercise prescription was the same for both sexes, women expended 200 kcal less energy and this might explain the results obtained. Furthermore, Stubbs and colleagues (2002a,b) have conducted a series of experiments aiming to elucidate the relationships between exercise, energy intake and EE in free-living individuals fed *ad libitum*. Healthy, normal weight males and females were studied under three 7-day treatments: sedentary routine, moderate-amount exercise and high-amount exercise. Women expended 9.2, 11.0 and 12.1 $MJ \cdot d^{-1}$ in each trial, while their energy intake was 8.9, 9.2 and 10.0 $MJ \cdot d^{-1}$ respectively. There was no treatment effect on appetite and body mass. In men ExEE amounted to 11.7, 12.9 and 16.8 $MJ \cdot d^{-1}$ and their corresponding values for energy intake were 11.6, 11.8 and 11.8 $MJ \cdot d^{-1}$. Although there was no effect on hunger, there was evident weight loss on the high-amount exercise treatment, exhibiting that women are more prone to energy intake compensation. Combining these data sets, however, showed that spontaneous activity EE declined as the study progressed on the higher amount exercise treatments in both genders. This decrease

amounted to an approximate compensation of 0.3-0.6 $MJ \cdot d^{-1}$ on the moderate- and high-amount exercise treatments in males and 0.3 $MJ \cdot d^{-1}$ on both moderate- and high-amount exercise treatments in females. A further study conducted by the same group, confirmed that males compensate for imposed exercise, with an approximate energy cost of 4 $MJ \cdot d^{-1}$, by reducing spontaneous activity EE (Stubbs et al., 2004a). The authors though concluded that this decline may be due to fatigue amounted during the exercise programme. Apart from that, these results should be considered with caution, since sample-size was particularly small and not representative of the whole population and menstrual cycle for women was not controlled. Furthermore, since both absolute and relative EE were different between males and females this could have resulted in different metabolic signalling pathways being activated, which may have resulted in different responses between the genders. In addition it was evident that there was a large interindividual variability, however, individual data on weight loss could not confirm the trend of compensation.

On the contrary, there is evidence from medium-term exercise studies to suggest that both men and women do not compensate by being less active outside a cycling exercise programme of 8 days (Mc Laughlin et al., 2006). In this study, where EE was assessed throught HR monitoring combined with physical activity records, men did not lose body weight either in control or in the exercise trial, but women lost weight in the exercise trial when measured at the same phase of their menstrual cycle. Therefore, differences between genders in relation to body mass reduction could be explained by the energy intake response to exercise; still it was claimed that evidence for difference between

individuals might be stronger than those existing between genders. Indeed, when the protocol of Stubbs et al., (2002a,b) was extended over 16 days (Whybrow et al., 2008) it was found that participants overall compensated for about 30% of the exercise-induced energy deficit. However, the degree of compensation varied considerably among individuals. This finding gave ground to the importance of individual response to energy expended during exercise. It was evident that people who behaved as "compensators" increased their energy intake in response to ExEE, while "noncompensators", showed no increase in energy intake. Individual behaviour towards energy balance components could therefore partly explain different results obtained among medium-term studies.

On the other hand, there is evidence to show that exercise does not elicit a change in energy intake; however the possibility of compensation in the form of decreased non-exercise EE is not excluded. Stubbs et al., (2004b) conducted a study in a whole body calorimeter suggesting that after 7 days of exercise and although hunger was increased, there was no impact on energy intake but this result was highly influenced by diet composition with high-fat diet resulting in higher energy intake than low-fat diet. In addition, Woo and Pi Sunyer, (1985; 1982a,b) compared obese and lean women who underwent three 19-day interventions of non, mild and moderate exercise under controlled conditions. They concluded that although energy compensation was not evident in obese, lean individuals compensated through increased energy intake. They suggested, however, that obese women may compensate for the increased EE by being less active during the rest of day (Woo and Pi Sunyer, 1982a,b). Another study on previously obese women proposed that eating habits as opposed to physiological signals

produced during exercise over 14 days have a greater influence on energy intake, leading individuals to either overeating or undereating (Keim et al., 1996).

Few medium-term studies have considered appetite in addition to energy balance components. Three studies found exercise on 7 consecutive days to significantly increase the feelings of hunger in lean sedentary males (Stubbs et al., 2004a, Stubbs et al., 2002a) and lean physically active females (Stubbs et al., 2002b). The study of Keim et al., (1996) on reduced obese females, however, found hunger to increase only in those who were characterised as overeaters. Despite the apparent potential of exercise to increase appetite, the evidence is limited and lacks strength as all four studies assessing the effects of appetite were based on small sample-sizes and were therefore prone to greater sample errors. On the contrary, Whybrow et al., (2008) found no effect on appetite but energy intake partially compensated for energy expended. Similarly, the study by Stubbs et al., (2004b), carried out in a whole-body calorimeter for accurate measurements of EE, showed no effect on appetite sensations.

Overall, medium-term exercise studies suggest that the relationship between appetite and energy intake is weak but apparently both energy intake and EE are potential mechanisms through which a compensatory effect in response to exercise may be exerted. However, as in short-term interventions, variations in experimental protocols, small sample-sizes, diverse populations studied and different modes and doses of exercise in the literature makes it difficult to draw clear conclusions. Therefore, long-term programmes of exercise which correspond better to “real-life” context may be

necessary to elucidate compensation mechanisms in order to design effective public health strategies for weight loss, weight maintenance and prevention of unhealthy weight gain.

In Table 2, eleven medium-term studies are presented of which:

- seven show that energy intake remained the same during the course of the study.
- four show an increase in energy intake
- four out of eleven suggest an increase in appetite sensations, while two out of eleven show no impact, but most of these findings were not accompanied by the same trend of change in energy intake
- two suggest spontaneous activity EE decreased during the course of the study.

1.4.3 Effect of long-term exercise programmes on appetite and energy balance

Studies to investigate the effect of long-term exercise programmes on appetite and energy balance are included in Evidence Table 2. To identify the articles included in Evidence Table 2, search engines of the databases MEDLINE and OVID were used for papers published from 1982 to 2010 in English using the terms “physical activity”, “exercise intervention”, “exercise programme”, “long-term exercise”, “fitness” together with “energy intake”, “*ad libitum* food intake”, “appetite”, “energy expenditure”, “energy balance”. The reference lists of articles retrieved were also examined. Papers were excluded if energy intake and/ or components of TEE were not measured, if participants were following specific diets and if duration of the exercise intervention was more than 16 months.

Long-term intervention studies lasting more than 4 weeks are the most valuable type of study in this area of research, as the results obtained can be applied directly to "real-life" exercise programmes. Studies lasting for duration of between 4 weeks to 16 months investigating components of energy balance in relation to body composition/ body mass changes during an exercise programme under free living conditions and habitual diet maintenance have been considered in this review. Such studies were conducted on both lean and obese, males and females and covered a range of exercise types including walking, cycling, running and resistance training of both high and low intensities.

Evidence provided from various well-controlled studies demonstrates that an increase in EE through exercise has the capacity to induce weight loss when energy intake is tightly controlled and maintained at baseline levels. For example, Ross et al., (2000) showed that a three-month exercise programme in which 16 obese men expended 700 kcal per day, 7 days a week, led to a reduction of 6.1 kg total body fat. Further evidence to show exercise to be a successful method of weight-loss has been provided by the long term randomised controlled trial, STRIDDE, which reported that exercise leads to weight loss in a dose-dependent manner in overweight and obese males and females, with those participants performing the greatest amount of exercise losing more than double the quantity of fat mass than those performing the least amount of exercise (Slentz et al., 2000).

When energy intake is not tightly controlled, however, literature unequivocally shows that body mass and/or fat reduction in response to exercise is often minimal compared

with caloric restriction and seldom reaches the predicted fat loss (King et al., 2009a,b; Church et al., 2009; King et al., 2008; Barwell et al., 2008; Martins et al., 2007b; Cox et al., 2003; Donnelly et al., 2003; Irwin et al., 2003; Potteiger et al., 2003; Donnelly et al., 2000; Mertens et al., 1998; Suzuki et al., 1998; Van Etten et al., 1997; Snyder et al., 1997; Westerterp et al., 1992; Broeder et al., 1992; Wood et al., 1991; Andersson et al., 1991; Keim et al., 1990; Leon et al., 1979). A meta-analysis of 493 studies carried out by Miller et al., (1997) has shown the weight reduction by means of exercise over a 3-4 month period in moderately obese individuals to be a minor 2.9 kg, compared to 10.7 kg weight loss achieved by caloric restriction alone. In addition, a long term randomised controlled trial carried out by Potteiger et al., (2003) found that an energy deficit of 1300-2200 kcal per week through moderate-intensity exercise, produced a total body fat reduction of approximately 2.5 kg over a period of 16 months. The observed fat loss was only 25% of the predicted fat loss (10 kg), calculated based on the estimated requirement of 7700 kcal to burn 1 kg of body fat (Wolfe, 2006). Although preservation of lean mass by exercise may be in part responsible for the difference in weight loss achieved by diet and exercise (Weiss et al., 2007), the minimum amount of fat mass lost with exercise, indicates the role of additional factors that may attenuate weight loss with exercise alone. Collectively, these findings demonstrate that whilst exercise has the capacity to induce body fat loss independently in overweight and obese individuals, in situations when caloric intake is not restricted or tightly controlled commonly observed in “real-life” exercise programmes, often considerably less weight loss than predicted is achieved.

Many studies investigating components of energy balance in relation to body composition changes show that exercise programmes have no impact on energy intake and thus it is assumed that no compensation is involved in response to exercise (Martins et al., 2010; Cox et al., 2003; Donnelly et al., 2003; Irwin et al., 2003; Van Etten et al., 1997; Suzuki et al., 1998; Broeder et al., 1992; Westerterp et al., 1992). As a result it would be expected that individuals enter a state of negative energy balance and achieve weight loss. However, anthropometric measurements have shown that weight loss was not always observed (Cox et al., 2003; Donnelly et al., 2003; Irwin et al., 2003; Van Etten et al., 1997; Broeder et al., 1992; Westerterp et al., 1992) suggesting either that in some cases the measure of energy intake is inaccurate and compensation did in fact occur through diet, or alternatively, compensation may have occurred through a reduction in daily EE.

Indeed, because of failure of participants to achieve expected weight loss, it has been suggested that exercise programmes due to the exercise-induced energy deficit at some critical point may trigger an increase in energy intake (Melzer et al., 2005), or may activate compensatory mechanisms in the form of a reduction in normal daily activities offsetting energy deficit created, thus maintaining energy balance and preventing weight loss (Blundell et al., 2003). This compensation for the exercise-induced energy deficit may explain why exercise alone often fails to result in successful weight loss in obese and overweight individuals (Franz et al., 2007). Long-term studies investigating the impact of exercise programmes on energy intake and TEE components can confirm that participants who do not achieve expected weight loss may experience an increase in

food intake (King et al., 2009a; King et al., 2008; Westerterp et al., 1992) or a reduction in normal daily activities (Stubbs et al., 2002a,b; Goran and Poehlman, 1992). The possibility that these two mechanisms work synergistically still exists, but no long-term studies up to date were able to demonstrate such an effect.

As far as gender differences are concerned, Donnelly et al., (2003) found obese men to significantly reduce body mass after a 16-month moderate exercise programme, whereas the body mass in obese women was not significantly different from baseline, despite no differences in recorded energy intake. It was noted by the authors, however, that the statistical power to detect a difference in energy intake in women was poor, with the possibility of underreporting confounding results. Despite lack of adequate energy intake data, this indicates women but not men tend to compensate for an energy deficit created through exercise. A similar scenario was observed by Westerterp et al., (1992) in which lean and overweight men and women underwent four exercise bouts per week for 44 weeks. Although no significant difference in energy intake measures was obtained in both genders, men tended to decrease energy intake in comparison to baseline as the study progressed, whereas women tended to increase energy intake, thus compensating for the exercise-induced EE. Consequently, a significant negative energy balance occurred in men by week 8, continuing to the end of the study at week 44, and no change in energy balance was observed in women.

Lately, interindividual variability of responses to exercise programmes has been observed by researchers (King et al., 2009a,b; King et al., 2008; King et al., 2007; Blundell et al., 2003; Donnelly et al., 2003), however, data evaluating individual

responsiveness to exercise-induced fat loss are very limited. Some studies have been conducted to show how individual behaviour is altered by energy balance perturbations, highlighting its importance for physical activity interventions aiming to weight management. Recent studies of King et al., (2009a,b; 2008) investigating mechanisms responsible for individual variability in body mass and body fat changes during exercise programmes in overweight individuals and measuring energy intake changes from *ad libitum* lunch and dinner meals, reported that over the course of exercise intervention some of the participants increased (nonresponders or compensators) and others decreased (responders or noncompensators) their energy intake, and that differences in energy intake changes contributed to the individual variability in body mass and body fat loss. Although, alterations in physical activity in non-exercise time were not properly investigated in these studies, it was exhibited that the effectiveness of exercise on weight loss is variable because participants tend to behave individually towards volitional compensatory responses and as such other individuals are prone to weight loss through exercise, while others are resistant. As the majority of studies have performed analysis on data collectively to obtain one mean value, the imbalance of "responders" and "nonresponders" in the volunteers pool may explain the varied weight loss observed in many of the long term studies (Donnelly et al., 2003; Irwin et al., 2003) and the failure to find a significant result altogether (Martins et al., 2007b; Cox et al., 2003; Van Etten et al., 1997). It is therefore possible that due to pooled analysis by the majority of studies investigating the impact of exercise on weight loss, current evidence may not reflect the real picture in terms of compensatory mechanisms, and does not identify whether the response to exercise is an individual effect with some individuals more prone than others

to compensating through increasing energy intake and decreasing spontaneous physical activity. Findings from other studies suggest that induced changes in energy balance may depend on the initial fat mass and lean individuals will compensate more after exercise as their body mass is threatened by the exercise-induced energy deficit (Blundell et al., 2003; Lim and Lee, 1994).

Only few studies have assessed appetite in response to long-term exercise by close observation in controlled environment at baseline and at the end of the intervention (Martins et al., 2010; King et al., 2009a; King et al., 2008; Martins et al., 2007b). In these studies participants either did not achieve overall any body mass and body fat change (Martins et al., 2007b) or actual body mass loss did not reach the level of predicted (Martins et al., 2010; King et al., 2009a; King et al., 2008). It could be inferred that there is a notion towards the acceptance of exercise as being able to influence appetite beneficially (Martins et al., 2010; King et al., 2009a; Martins et al., 2007b; Long et al., 2002) through a dual process action. King et al., (2009a) suggested that exercise might be able to increase the overall orexigenic drive, but at the same time can improve meal-induced satiety and in this way protect some individuals from energy overconsumption.

Unfortunately, different experimental protocols and exercise modes used by long-term studies, makes it difficult to draw clear conclusions. One point to consider when reviewing the results of long-term interventions is the risk of underreporting confounding the results. Unlike the shorter term interventions, most long-term studies

measure energy intake from self-reported intake of the participant, which relies on their honesty and ability to record food consumed accurately. Although a practical method, it has often been associated with under and misreporting, particularly in obese individuals (Heitmann and Lissner, 1995; Samuel-Hodge et al., 2004), but also in lean subjects (Van Etten et al., 1997), which can underestimate the true measure of energy intake by up to 50% (Cox et al., 2003).

Another reason that could be accounted as a factor for the exercise failure as means of weight reduction is compliance to exercise programmes. Increased adherence to prescription of exercise is associated with both overall weight loss as well as fat mass loss in a group of obese women undergoing a structured lifestyle intervention programme (Colley et al., 2008; Donnelly et al., 2003). Additionally, when regimens are completed as prescribed, there remains little doubt that they can be associated with health benefits and predictable weight loss (Slentz and Duscha, 2004; Jeffery and Wing, 2003; Ross et al., 2003; Ross and Freeman, 2002; Ross and Dagnone, 2000). However, within the context of large-scale exercise interventions, it is often unrealistic to supervise the exercise training of the participants and thereby have high confidence in the true dose of exercise completed. The most common way adherence can be monitored is the use of heart rate monitors and/ or accelerometers. Nevertheless, unsupervised exercise sessions increase the variability in weekly ExEE indicating that some participants engaged in little or no exercise, whereas others surpassed the prescribed dose and this could have huge impact at the results and their translation within exercise interventions. Realistically also when unsupervised, it is rather difficult for individuals to motivate

themselves to undertake regular exercise of appropriate intensity and duration to gain benefit (Colley et al., 2008).

Overall, evidence to explain why long-term exercise interventions not accompanied by energy intake restriction fail in most cases to induce predicted body mass loss is limited and contradictory. It is imperative therefore, that research focuses on the obstructive compensatory mechanisms evident in exercise programmes on the individual basis.

In Table 2, thirteen long-term studies are presented of which:

- seven show that exercise intervention had no impact on energy intake, however six out of seven suggest that weight loss was not observed.
- two show that energy intake decreased following an exercise intervention.
- three conclude that those who do not achieve predicted weight loss increase energy intake.
- four report no impact of exercise intervention on spontanous activity EE.

Evidence Table 2. Studies assessing the effect of medium- and long-term exercise programmes on appetite and energy balance

Name	Subjects	Duration	Intervention	Main Outcome	Results	Conclusion	Comments
Martins *et al.*, 2010	22 men and 14 women (15 men and 7 women finally completed the study) Healthy Mean age (y): 36.9 ± 8.3 Mean BMI ($kg \cdot m^{-2}$): 31.3 ± 3.3 Mean BF (%): 35.3 ± 5.6 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): 32.9 ± 6.6	12 wk ex training on acute appetite control	Ex: 12 wk of walking or running (500 kcal/session, 5d/wk at 75% HRmax) At baseline and wk 12: A fixed breakfast and follow up for 3 h with frequent measurements	BW and BC Appetite sensations RMR Habitual EI Glucose, insulin, total ghrelin, AG, PYY, GLP-1	Ex resulted in a sig reduction in BW and fasting insulin and an increase in AG plasma levels and fasting hunger sensations A sig reduction in postprandial insulin plasma levels and a tendency toward an increase in the delayed release of GLP-1 (90–180 min) were also observed after ex, as well as a sig increase (127%) in the suppression of AG postprandially	Ex-induced wt loss is associated with physiological and bio psychological changes toward an increased drive to eat in the fasting state. However, this seems to be balanced by an improved satiety response to a meal and improved sensitivity of the appetite control system.	Supervised sessions (avr compliance: 89 ± 5.9%) Mixed effect on both men and women Normal diet kept throughout the study, verified with 3-d estimated EI diary before and after Large dropout rate BC was measured with DEXA Fixed meal only effect

King *et al.*, 2009a	58 OW and O men (n=19) and women (n=39) Healthy, sedentary Mean age (y): 39.6 ± 9.8 Mean BMI ($kg \cdot m^{-2}$): 31.8 ± 4.8 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): 29.1 ± 5.7	12 wk ex training on acute appetite control	Ex: 12 wk of a range of aerobic ex ergometers (2500 kcal/wk; 500 kcal/ session; 5 d/wk @ 70% HRmax) At baseline and wk 12: A fixed breakfast and 3 ad libitum meals (lunch, dinner, snack) were given and EI, appetite were measured in the postprandial period throughout the day	BW and BC Appetite sensations Satiety quotient EI EB Analysis of individual response	After 12 wk, in the group as a whole there was sig reduction in mean body weight (3.2 ± 3.6 kg), fat mass (3.2 ± 2.2 kg), and WC (5.0 ± 3.2 cm). Fasting and average hunger across the day increased sig ($p < 0.0001$). Immediate and delayed satiety quotient of the breakfast also increased sig ($p < 0.05$) When participants were divided in responders (R) and nonresponders (NR) based on actual and predicted weight loss 9 women and 10 men were R to the exercise programme. R decreased EI (-125 kcal/d), increased fasting hunger and had the same satiating efficiency with NR Non-exercise PA was not different between R and NR but was measured only on probe days every 4 weeks with accelerometers (data not shown)	12 wk of ex induced favourable changes in BC, increased the satiating efficiency of a fixed meal and the overall orexigenic drive to eat in OW and O population.	Supervised sessions (avr compliance: 89.1 ± 10.7%) Mixed effect on both men and women Probe day food measurement protocol used, including a fixed breakfast Compensation (actual - predicted wt loss) Calculations were based on assumed energy costs of 9540 and 1100 kcal/kg FM and FFM, respectively Both R and NR experienced sig changes in BW, FM, and WC BC measured with Bodpod
King *et al.*, 2009b	58 OW and O men and women	12 wk ex intervention	Ex: 12 wk of a range of aerobic ex ergometers	BW and BC BP	The mean reduction in body weight was 23.3 ± 3.63 kg, ($p<0.01$)	Ex can exert meaningful health benefits	Same pool of subjects as King et al., 2009a?

	Healthy, sedentary Mean BMI (kg·m^{-2}): M: 30.5 ± 3.3 F: 32.6 ± 4.8		(2500 kcal/wk; 500 kcal/ session; 5 d/wk @ 70% HRmax) Measurements obtained at baseline and wk 12	Resting HR VO_2max Acute affective response to ex (PANAS)	However, 26 of the 58 participants failed to attain the predicted wt loss estimated from individuals' ExEE. Their mean weight loss was only 20.9 (1.8) kg ($p<0.01$). But sig increases in aerobic capacity (6.3 ± 6.0 ml/kg/min; $p<0.01$), and a decreased systolic (26.00 ± 11.5 mm Hg; $p<0.05$) and diastolic blood pressure (23.9 ± 5.8 mm Hg; $p<0.01$), WC (23.7 ± 2.7 cm; $p<0.01$) and resting HR (24.8 ± 8.9 bpm, $p<0.001$). In addition, these individuals experienced an acute ex induced increase in positive mood	even in the presence of lower-than-expected ex-induced wt loss. A less successful reduction in BW does not undermine the beneficial effects of aerobic ex.	Supervised sessions Mixed effect on both men and women Normal diet kept throughout BC measured with Bodpod
Church *et al.*, 2009	411 women Healthy, sedentary, postmenopausal Mean age (y): 57.2 ± 6.3 Mean BMI (kg·m^{-2}): 31.7 ± 3.8 Mean VO_2max (ml·kg^{-1}·min^{-1}): 15.6 ± 2.8	6 mon ex intervention	Randomized, dose-response ex trial with 4 groups: 1. Control (n= 94) 2. Ex (4/kcal/kg/wk) (n=139) 3. Ex (8/kcal/kg/wk) (n=85) 4. Ex (12/kcal/kg/wk) (n=93) Ex: 6 mon cycling ex intervention (3-4 training	BW and BF EE Fitness WC	The mean (95% CI) wt loss in the 4, 8 and 12 KKW groups was 21.4 (22.0, 20.8), 22.1 (22.9, 21.4) and 21.5 (22.2, 20.8) kg, respectively In the 4 and 8 KKW groups the actual wt loss closely matched the predicted wt loss of 21.0 and 22.0 kg, respectively, resulting in no sig compensation In the 12 KKW group the actual wt loss was less than the predicted wt loss (22.7 kg) resulting in 1.2 (0.5, 1.9) kg of compensation (<0.05) compared to 4 and 8 KKW groups All ex groups had a sig reduction in WC which was independent of	No difference in the actual and predicted weight loss with 4 and 8 KKW of ex (72 and 136 min respectively), while the 12 KKW (194 min) produced only about half of the predicted wt loss. However, all ex groups had a sig reduction in	Multi ethnic participants Good adherence Supervised sessions (higher adherence in lower amount of ex) Compensation (actual - predicted wt loss). Predicted weight loss (ExEE/ 7700 kcal/ kg) Non-exercise PA

			sessions/wk at 50% of VO_2max, incremental protocol)		changes in wt Dose response change in fitness (p-trend <0.001) No difference in non exercise PA and BF among groups	WC which was independent of changes in wt.	was not different but was measured throughout intervention with step counters only on probe days every 4 weeks with accelerometers (data not shown) BW measured with electronic scales and BF by 4 skinfolds
Whybrow *et al.*, 2008	6 men 6 women Healthy, sedentary to moderately active Mean age (y): M: 29.7 ± 5.9 F: 24.7 ± 5.9 Mean BMI ($kg \cdot m^{-2}$): M: 24.2 ± 2.2 F: 22.9 ± 1.6 Mean BF (%): M: 19.3 ± 4.4 F: 29.9 ± 1.7	16 d ex intervention	Participants randomised to 3 x 16 d protocol: 1. Con (No Ex), 2. MI ex (2x40 min session/d ; 1.5–2 MJ/d) 3. HI ex (3x40 min session/d; 3–4 MJ/d) Days 1-2: fed to EB Days 3-16: ad libitum feeding of constant composition and ex cycle or treadmill ergometer	BW and BF EE and components EI/ macronutrient intake EB Appetite sensations	Daily EE sig increased and was 9.2, 11.6 and 13.7 MJ/d (p<0.001) for the women and 12.2, 14.0 and 16.7 MJ/d (p=0·007) for the men on the Nex, Mex and Hex treatments, respectively EI did not increase 8.3, 8.6 and 9.9 MJ/d (p=0.118; SED 0.72) in women but sig increased 10.6, 11.6 and 12.0 MJ/d (p=0·031; SED 0·47) in men Non-ex EE (calculated from total EE – ExEE) was not affected by the ex intervention There were no sig differences in BW in FFM, FM or BF across the three treatments for the women or the men No significant treatment effects for appetite in both genders	Participants compensated for about 30% of the ex-induced energy deficit. However, the degree of compensation varied considerably among individuals. The present study captured the initial compensation in EI for ex-induced energy deficits. Total	Small sample size Participants resident in lab but not confined in Daily TEE assessed with DLW BW measured by scales and BF by skinfolds ExEE from HR-FLEX Compliance to ex checked with HR monitors

					Increased fluid intake in response to exercise	compensation would take a matter of weeks.	
King *et al.*, 2008	35 OW and O men (n=10) and women (n=25) Healthy, sedentary Mean age (y): 39.6 ± 11.0 Mean BMI ($kg \cdot m^{-2}$): 31.8 ± 4.1	12 wk ex intervention on acute appetite control	Ex: 12 wk of a range of aerobic ex ergometers (2500 kcal/wk; 500 kcal/ session; 5 d/wk @ 70% HRmax) At baseline and wk 12: A fixed breakfast and 2 ad libitum meals were given and EI, appetite were measured in the postprandial period throughout the day	BW and BC Appetite sensations RMR EI SQ Analysis of individual response	<u>Pooled data:</u> Mean BW reduction: (3.7 ± 3.6 kg), ($p<0.0001$) and as predicted, which suggested no compensation for the increase in EE <u>Individual data</u> Further examination revealed a large individual variability in wt change (-14.7 to +1.7 kg). Subjects were identified as compensators (C) or noncompensators (NC) based on their actual wt loss (mean NC=6.3 ± 3.2 kg and C=1.5 ± 2.5 kg) relative to their predicted wt loss Moderate changes in RMR occurred in C (-69.2 ± 268.7) and NC (14.2 ± 242.7) kcal/d EI and average daily subjective hunger increased by 268.2 ± 455.4 kcal/day and 6.9±11.4 mm/day in C, whereas EI decreased by 130±485 kcal/day and there was no change in subjective appetite (0.4±9.6 mm/day in NC Satiating effect of the fixed breakfast increased over the 12-wk period of ex. This effect was maintained for 4 h after the meal	Expressing the ex-induced change in BW as a group mean conceals the large inter-individual variability in BW and compensatory responses. Individuals who experience a lower than predicted weight loss are compensating for the increase in EE by eating more.	Supervised sessions (completed sesions: 89.1 ± 10.7%) Mixed effect on both men and women Compensation (actual - predicted wt loss). Predicted weight loss (ExEE/ 7700 kcal/ kg) BW and BC measured by BIA

Martins *et al.*, 2007b	15 men 14 women Healthy, sedentary Mean age (y): 29.8 ± 11.6 Mean BMI ($kg \cdot m^{-2}$): 22.7 ± 2.3 Mean restraint/external/ emotional eating: 2.2 ± 0.7/ 2.5 ± 0.7/ 3.0 ± 0.5 respectively	6 wk ex training on acute appetite control	Randomised single-blind cross-over design 2+2 EI trial: 1. High energy preload (HEP) 2. Low energy preload (LEP) Exercise: 6 wk ex intervention either in gym or cycling at home (4 times/wk, 30-45 min, 65-75% HR max) Preceded by set breakfast and preload and followed by ad libitum buffet meal. Appetite and EI were measured in the postprandial period throughout the day	BW and BC Fitness Metabolic variables (HDL-chol, TG, NEFA, glucose, insulin) EI and macronutrient intake over 24h and at buffet lunch Habitual EI Subjective appetite sensations	Fitness sig improved with ex in all participants ($p<0.05$) No sig changes in BW and BC and blood metabolites after the exercise intervention After the ex intervention all participants and men group sig downregulated cumulative EI over 24h after the HEP compared with the LEP ($p<0.05$) Hunger increased sig after the preload at baseline and after the ex intervention Fullness increased immediately after the preload and decreased thereafter in both at baseline and at the end of the study No effect of ex programme on macronutrient intake, EI	Increasing habitual PA levels in previously sedentary individuals has an impact on short-term appetite regulation and compensation. PA may not only increase EE but also lead to a favourable more sensitive eating behaviour.	Not supervised sessions (women complied better than men) Power not enough to show differences between gender Mixed effect on both men and women Participants could take leftovers home and record EI till next morning BC measured by BIA Normal diet kept throughout the study EI measured with 3d and 24 h food recall at 0, 3 and 6wk Pedometers worn for a week, before the start of the study, at weeks

							3and 6 of the ex programme to ensure no compensatory reduction in non-ex PA
Mc Laughlin *et al.*, 2006	8 men 8 women Healthy Mean age (y): M: 23 ± 1 F: 24 ± 3 Mean BMI ($kg \cdot m^{-2}$): M: 25.3 ± 5.3 F: 21.9 ± 1.6 Mean BF (%): M: 18.6 ± 7.4 F: 17.5 ± 3.5 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): M: 44 ± 8 F: 40 ± 5	16 d ex intervention	In counterbalanced order: 1. Con (8 d of habitual physical activity) 2. Ex (8 d imposed ex) Ex: cycling was conducted every 2nd d, each consisting of a total net EE of 2092 kJ + BMR at 90% LT	BW and BC TEE and components	During the Ex period, TEE was higher than Con in M and F (Ex: 95.27 ± 13.9, 78.37 ± 15.9 MJ; Con: 82.47 ± 10.4, 68.87 ± 16.7 MJ, respectively; p=0.02) SAEE, (TEE-ExEE) was not sig different between Con (M: 82.47 ± 4.8 MJ; F: 68.87 ± 7.6 MJ) and Ex (M: 86.87 ± 6.3 MJ; F: 70.07 ± 7.2 MJ) periods in either gender Males showed no change in BM over the Con (pre-intervention: 83.47 ± 7.2 kg; post-intervention: 83.17 ± 6.8 kg) or Ex (pre-intervention: 83.47 ± 6.8 kg; post-intervention: 83.47 ± 6.8 kg) periods F' BM over the Con period did not alter (pre-intervention: 63.37 ± 2.8 kg; post-intervention 63.77 ± 3.1 kg); however, there was a sig decrease (p<0.00) in BM over the Ex period (pre-intervention: 63.07 ± 2.7 kg; post-intervention: 62.47 ± 2.7 kg)	The ex programme was achieved in males and females without any impact on SAEE. Therefore, differences between genders in relation to BM reduction can be explained by differences in the EI response to ex .	Supervised ex session Menstrual cycle accounted for ExEE and TEE measured by combined method of diaries+ HR to VO_2/VCO_2 BW was measured by digital scales and BC by skinfolds
Stubbs *et al.*, 2004a	8 men	7 d ex intervention	Cross over design 7 days per trial,	Appetite sensations	<u>Mean ExEE (kcal/d)</u> HFEx: 1170	Sig increase in hunger in	HF diet: 50% energy from fat

	Healthy, moderately active Mean age (y): 29.5 ± 6.0 Mean BMI ($kg \cdot m^{-2}$): 23.9 ± 2.2 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): 42.2 ± 9.88		2x2 randomised design 1. HF diet with Ex (HFEx) 2. HF diet no Ex (HFNEx) 3. LF diet with Ex (LFEx) 4. LF diet no Ex (LFNEx) Exercise: 7 d ex intervention (3x40min session/d at ~65% VO_2max) During 7 d ad libitum access to 3d rotating menu	BW and BC TEE and components EI Cumulative EB over 7 days	LFEx: 1098 No sig difference between trials <u>Mean EE and EI</u> (kcal/d) EE EI HFEx 4251 3343 HFNEx 2913 3057 LFEx 4155 2221 LFNEx 2579 2101 Mean daily EE was sig greater in Ex than no Ex trials ($p<0.001$) No sig difference in EI between Ex and no Ex trials, or from day 7 compared to baseline. Sig greater EI in HF compared to LF trials ($p<0.001$) <u>Mean EB</u> (kcal/d) Day1 Day7 Ex -1671 -1194 N-Ex 0 -238 LF -1433 -1074 HF -238 -358 Sig increase in hunger and desire to eat in Ex compared to No Ex trial ($p<0.05$) and in the LF compared to HF trials ($p<0.05$)	response to ExEE, but no impact on EI over the 7 d. The ExEE caused negative EB caused a compensatory reduction in daily EE. Results suggest state of EB largely influenced by diet composition with a HF diet resulting in sig higher EI than LF diet which may therefore compensate for ex-induced energy deficit.	LF diet: 25% energy from fat EI measured through weighed intake by investigators BC measured by skinfolds TEE by FLEX HR -2 -1 d maintenance diet Daily EE (not incl. ExEE) sig decreased during course of study in Ex trials ($p=0.02$) and in LF trials ($p=0.045$) but not in the HFNEx trial Sig reduction in EI in HF but not LF trials at day 7 compared to baseline BW loss (Kg): HFNex: -0.19 HFex: -0.31 LFex:-0.33 LFNex: -0.68

Stubbs *et al.*, 2004b	6 men Healthy, physically active Mean age (y): 23 ± 2.3 Mean BMI ($kg \cdot m^{-2}$): 22.2 ± 2.4	7 d ex intervention	Cross over design, 7 days per trial with continuous whole-body calorimetry 1. Sedentary regime (2x40min p/d 60W, PAL:1.4) 2. Active regime (3x40min p/d 90W, PAL:1.8) Ex: Cycling Ad libitum feeding of medium-fat diet throughout 7 d	Appetite sensations EE EI BW Cumulative EB over 7 days	<u>Mean TEE (kcal/d):</u> Sedentary: 3050 Active: 2328 Sig greater TEE in active compared to sedentary regime ($p<0.001$). Total cumulative difference in TEE after 7 days (kcal): + 5015 in Active <u>Mean EI (kcal/d):</u> Sedentary: 3427 Active: 3224 EI did were not sig different between trials. No sig difference in appetite ratings between trials <u>Cumulative EB over 7 day period (kcal):</u> Sedentary: +6281 Active: +2651 EB after 7 days was sig different from zero in sedentary regime only ($p<0.001$)	The active regime had no impact on hunger or EI compared with sedentary regime. Subjects entered positive EB in both trials, but to a greater extent on sedentary regime due to the sig lower daily TEE with no compensatory EI reduction. Ex therefore attenuated development of positive EB due to ExEE without EI compensation.	Subjects blinded to the true aim of study EI measured by weighed intake by investigators Subject habitual PAL approx: 1.7 Small sample size, non-random sample, subjects may not be representative of general population, study wasn't free living, not completely free choice of diet BW increased by ~ 0.66kg on active regime and 0.9kg on sedentary regime over 7 day period. Sig different from zero only in sedentary ($p<0.001$)
Donnelly *et al.*,	31 men 43 women	16 mon ex intervention	Randomised control trial	BW and BC	<u>MEN</u> <u>Mean ExEE (Kcal p/session)</u>	Despite an increase in	EI measured through weighed

2003	Healthy, sedentary Mean age (y): 17-35 Mean BMI ($kg \cdot m^{-2}$): 25-34.9		1. Con 2. Ex: walking at 55-60% VO_2max Duration gradually increased from 20 min at baseline to 45 min 5x p/wk at 6 mon. Target of EE: 400 kcal /session achieved in first 6 mon then maintained for 2nd 6 mon	ExEE EI	≤5wk: 400 5-13 wk: 550 30-66 wk: 650 ExEE sig increased between wk 5 and 13 and wk 13 and wk 30 ($p<0.05$) <u>Mean EI</u> (kcal/d) Con Ex 0 mon 3524 ± 761 3084 ± 564 3 3431 ± 794 2865 ± 525 6 3331 ± 848 2985 ± 635 9 3514±1010 3029 ± 697 12 3242 ± 748 2973 ± 780 16 3433 ± 760 3156 ± 787 No Sig difference in EI between Ex and Con <u>WOMEN</u> <u>Mean ExEE (kcal p/session)</u> ≤5wk: 275 5-13 wk: 375 30-66wk: 430 ExEE sig increased between wk 5 and 13 and wk 13 and wk 30 ($p<0.05$) <u>Mean EI (Kcal/d)</u> (kcal/d) Con Ex 0 mon 2363 ± 503 2554 ± 580 3 2452 ± 582 2494 ± 405 6 2372 ± 524 2490 ± 452 9 2386 ± 850 2389 ± 463 12 2336 ± 644 2397 ± 629	ExEE, there was no effect on EI in either men or women compared to baseline and compared to Con. However, by 16 mon Ex group had sig lower BM, FM, BMI in both men and women compared to Con, as well as an increase in maximal O_2 consumption. BM in women was not sig different from baseline suggesting EI compensation.	intake of ad lib food consumption for 2 wk in cafe on 6 different occasions, as well as mutliple 24h recalls during study. BW measured by digital scales and BC by hydrostatic weighing VO_2 max increased in ex group In men, by 16 mon sig greater reduction in BM (5.2±4.7kg), ($p \leq 0.01$), FM (4.9±4.4kg), ($p=0.01$), BMI (1.6±1.4), ($p=0.02$) in Ex compared to Con In women, BM and BMI did not change sig in Ex group but sig increased in Con by 2.9±5.5kg and 1.1±2.0

					16 2464 ± 594 2418 ± 521 No Sig difference in EI between Ex and Con		respectively. FM in Con sig increased by 2.1±4.8kg in Con but remained relatively stable in Ex At end of trial, women in Ex group had sig lower BM, BMI, FM compared to Con ($p<0.05$)
Cox *et al.*, 2003	51 men Healthy, sedentary Mean age (y): 42.4 ± 5.0 Mean BMI ($kg \cdot m^{-2}$): 31.1	16 wk ex intervention	Randomised control trial, 2-way factorial design Assigned to low EI (LEI) or to continue with normal diet (NEI) in addition to light or vigorous ex: 1. LEI + LI Ex 2. LEI + HI Ex 3. NEI + LI Ex 4. NEI + HI Ex LI-Ex: slow flexible exercises 1x p/wk + cycling or slow walking	BW and BC EI	<u>Mean EI at baseline</u> (kcal/d) EI NEI LI-Ex 2303 (1855 to 2752) NEI HI-Ex 2177 (1811 to 2543) LEI LI-Ex 2434 (2092 to 2776) LEI HI-Ex 2558 (2191 to 2930) <u>Mean EI after 16 wk</u> (kcal/d) EI NEI LI-Ex 2216 (1954 to 2478) NEI HI-Ex 2319 (1868 to 2770) LEI LI-Ex 1473 (1246 to 1701) LEI HI-Ex 1403 (1170 to 1627) Sig lower EI post trial compared to pre-trial in LEI LI-Ex ($p<0.01$) and LEI HI-Ex ($p<0.001$) trials, but not in normal EI trials	ExEE had no effect on EI and did not enhance the reductions in BM, FM, and FFM, observed with energy restriction alone.	EI measured through self recorded 3 d weighed intake every 2 wk 24% increase in O_2 consumption with HI-Ex ($p<0.01$). No sig difference in LI-Ex Ex had no sig independent effect on BM, FM, or FFM. Energy restriction sig reduced BM, FM and FFM ($p<0.01$)

			2x p/wk HI-Ex: cycling for (3x30 min p/wk at 60% VO_2max)				Low Energy group subjects were heavier at baseline than normal energy groups – possible confouding Possible under-reporting as there was no change in BC or BM. Alternatively, possible daily EE compensation
Irwin *et al.*, 2003	173 women Healthy, sedentary, postmenopausal Mean age (y): 61 ± 2.8 Mean BMI ($kg \cdot m^{-2}$): 30.5 ± 1.8 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): 20.2 ± 1.2	12 mon ex intervention	Randomised controlled trial 1. Con (45mins stretching p/wk) 2. MI- Ex (45mins approx. 3.5d/wk) Ex: occurred both at study facility and home. Involved 1 or more of 38 activities including treadmill walking, cycling, strength training, jogging, walking, aerobics	BW and BC EI	Difference in EI from baseline to 3 mon (kcal/d) Con: -151 (-246 to -55) Ex: -155 (-250 to -60) Sig reduction in EI in both Con and Ex from baseline, but difference between groups were not sig Difference in EI from baseline to 12 mon (n=168) Con: -116 (-232 to 0) Ex: -37 (-152 to 79) Sig decrease in EI from baseline in Con but not in Ex. Difference between EI at 12 mon in Con and EX was not sig MI-Ex resulted in sig reduction (from baseline) in BW, BMI, WC, BF, hip circumference, subcutaneous and	MI-Ex for 45 min approx. 3.5 days p/wk led to a reduction in EI after 3 mths that was sig different from baseline, but not sig different from Con. By 12 mon, there was no sig change in EI in Ex group from baseline, indicating no compensatory effect of EI in	Walking and cycling was the main Ex involved BW was measured by balance beam scales and BC by DEXA EI recorded through FFQ taken at 0,3,12 mon Unable to determine EE due to missing data on duration of PA

					intra-abdominal fat, as well as increasing fitness, compared to control	response to ExEE.	
Stubbs *et al.*, 2002a	6 men Healthy, moderately active, unrestrained Mean age (y): 31 ± 5.0 Mean BMI ($kg \cdot m^{-2}$): 23.3 ± 2.4 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): 39.5 ± 1.5	7 d ex intervention	Cross over design, 7 days per trial 1. Con 2. M-Ex (2x40 mins p/d at 44% VO_2max) 3. H-Ex (3x40mins Ex p/d at 50% VO_2max) Ex: cycling Ad libitum access to normal diet for following 7 days	Appetite sensations BW EE EI EB	Mean EE (kcal/d) ExEE Daily -.ExEE Con 0 2794 M-Ex 621± 47 2460 H-Ex 1120 ± 71 2890 Sig greater daily EE in H-Ex trial than M-Ex or Con (incl. ExEE) ($p<0.001$). No sig differences in EE (excl. ExEE) Mean EI -EB (kcal/d) EI EB Con 2770 -23 M-Ex 2818 -238 H-Ex 2818 -1242 No sig difference in EI between trials. In M-Ex, but not H-Ex or Con, EI declined sig as study progressed ($p=0.014$) Sig different EB in H-Ex compared to M-Ex and Con ($p<0.001$) Ex had no sig effect on hourly hunger ratings, but End of Day questionnaire detected sig but small increase in perception of hunger in Ex trials ($p=0.08$)	ExEE resulted in a small but significant increase in hunger in both Ex trials but had no impact on EI leading to negative EB in the exercise trials. Slight compensation may have occurred through the decline in daily EE.	Subjects blinded to purpose of study EI measured by self recorded weighed intake (PETRA) for 7 days EE was measured by HR method Free living. Consumed normal diets – were not given funds or instructions on what to eat No sig difference between macronutrient percentage of diet between trials, but M-Ex consumed sig more energy-dense snacks than Con or H-Ex Although no sig difference in BW

							loss between trials or from zero, estimating EB from EI-EE was considered more precise Sig decline in daily EE (not incl. ExEE) as study progressed in M-Ex ($p=0.0015$) and H-Ex ($p=0.031$). Possible compensation, but also may be due to fatigue as opposed to EB regulation
Stubbs *et al.*, 2002b	6 women Healthy, physically active, unrestrained Mean age (y): 23 ± 0.6 Mean BMI ($kg \cdot m^{-2}$): 21.4 ± 1.0 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): 33.4 ± 2.5	7 d ex intervention	Cross-over design 7 days per trial 1. Con 2. M-Ex (2x40min p/d) 3. H-Ex (3x40min p/d) Ex: cycling Ad libitum access to normal diet	Appetite sensations EE EI EB	Mean EE (kcal/d) ExEE Daily-ExEE Con 0 2197 M-Ex 453 2149 H-Ex 812 2077 Sig graded increase in ExEE ($p<0.001$). Sig increase in daily EE (incl.ExEE), ($p=0.02$). No sig difference in daily EE (excl. ExEE) Mean EI -EB (kcal/d) EI EB Con 2125 - 71 M-Ex 2197 - 406 H-Ex 2388 - 501	ExEE resulted in a small but significant increase in hunger in both Ex trials, but only partial EI compensation occurred in H-Ex. All subjects therefore had a negative EB in Ex trials.	EI was self recorded weight intake using PETRA scales EE was measured by HR method As study progressed, daily EE decreased by 47 kcal in Ex trials compared to Con suggesting compensation for ExEE. Alternatively, may

					Sig greater EI in Hex compared to Con ($p=0.03$), but only ~30% compensation of ExEE. EB in Ex trials sig different from zero. Ex had no sig effect on hourly hunger ratings, but End of Day questionnaire detected sig but small increase in perception of hunger in Ex trials compared to Con ($p=0.08$)		be due to fatigue as opposed to EB regulation BW loss of -0.4kg in Con, -0.5kg in L-Ex, -0.8kg in H-Ex Normal diet kept throughout the study
Suzuki *et al.*, 1998	31 women Healthy, sedentary Mean age (y): 19.8 ± 0.2 Mean BMI ($kg \cdot m^{-2}$): 21.5 ± 0.4 Mean BF (%): 25 ± 1.2 Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): 36.2 ± 1.1	12 wk ex intervention	All subjects carried out 2 wk control period (no Ex) followed by 12 wk Ex regime Ad lib food intake throughout study Ex: cycling (5x30 min p/wk at 40% VO_2max)	BW and BC EE EI EB	Mean ExEE (kcal p/session): 117.5 ± 3.1 Mean EI (kcal/d) Control period: 1889 ± 44.9 Ex: 1876 ± 42.7 No sig difference in EI during Ex regime compared with during the control period %change in EI between control and Ex periods was sig negatively correlated with: EI in control period ($r=-0.604$, $p<0.05$); initial BMI ($r=-0.413$ $p<0.05$); initial %FM ($r=-0.39$, $p<0.05$)	Despite increase in EE due to Ex, there was no sig difference in EI during Ex compared to control period, and therefore subjects entered negative EB, with a significant reduction in body mass over the 12 wk.	EI measured through self recorded weighed intake, 14 days prior control period and 84 days throughout study. BM, BMI and FM sig decreased (-1.9kg, -1.9, -3.7kg respectively ($p<0.05$)). Sig negative correlations between %change and initial levels for BM ($r=0.045$ $p<0.05$) and FM ($r=0.638$ $p<0.05$). %change in EI is

							sig negatively correlated with EI in control period, initial BMI, %FM indicating that the extent to which EI is influenced by Ex may be dependent on the initial characteristics of the individual i.e. larger BMI is less likely to increase EI in response to ExEE
Van Etten *et al.*, 1997	26 men 18 men (Ex) 8 men (Con) Healthy, lean, sedentary Mean age (y): Ex:33 ± 6 Con: 35 ± 6 Mean BF (%): Ex: 19.1 ± 4.7 Con: 17.7 ± 6.1	18 wk ex intervention	Randomised control trial Each trial carried out 2x p/wk for 18 wk 1.Con 2.Ex (Mean duration: 72 min) Ex: weight training inc. bench press, squat, dumbbell curl, sit ups etc. Effects of a longitudinal	BM and BC components TEE and components EI	Mean ExEE and daily EE (kcal/d) ExEE Daily-ExEE Wk 0 n/a 2961 ± 286 Wk 8 102 ± 47 3122 ± 310 Wk 18 114 ± 35 311p ± 453 No sig difference in ExEE between wk 8 and wk 18. Sig increase in daily EE in wk 8 with no further increase by wk 18 ($p<0.001$). Mean increase in 18 wk period of total daily EE: 9.5% Mean EI (Kcal/d) (kcal/d) Con Ex Wk 0 2412±621 2412±429 Wk 8 2245±429 2316±429 Wk 18 2412±358 2197±453	ExEE through 2 sessions p/wk for 18 weeks increased daily EE by approx. 9.5% due to ExEE, with no effect on EI. However, EI was considerably and increasingly under-reported and therefore effects on EI of this	Main factor of compensation not stated Results based on 12 subjects in which EE was measured using DLW EI estimated via 3x3-day food record carried out weeks 0, 8, 18 No sig change in BW in Ex or CON after 18 wks

			weight training programme on daily metabolic rate (ADMR) and components of TEE Before, on wk 8 and wk 18 BC, SMR, EI (3-day food record), ExEE and SAEE (accelerometry-diaries) were measured ADMR measured on ex subgroup (n=12) by DLW		No sig difference in EI over 18 wk compared to baseline in Ex or Con. No sig difference between Ex or Con BM did not change sig in both groups Fat-free mass increased sig in Ex group Fat mass decreased sig in both groups ADMR increased sig at wk 8 and stayed stable thereafter SMR and EI (underreported) intake did not change sig in both groups ExEE could explain 40% of ADMR increase SAEE did not change sig in both groups	intervention are not conclusive. Weight training programmes of modest energy cost, induce a sig increase in ADMR	EE measured by DLW EE on PA (not incl. Ex session) did not sig differ across the 18 wks or between CON Under-reporting gradually increased during study - sig greater at wk 18 than baseline ($p<0.05$) BW was measured by electronic scales, BC by hydrostatic weighing and EE accelerometry
Keim *et al.*, 1996	15 women Healthy, sedentary, restrained, reduced obese Mean age (y): 31 ± 2 Mean BMI ($kg \cdot m^{-2}$): 28.7 ± 1.2 Mean BF (%): 38.7	14 d ex intervention	<u>Stage 1 (2wk):</u> Controlled dietary intake – caloric restriction for continuation of weight loss <u>Stage 2 (3.5wk):</u> Controlled dietary intake – EI to maintain weight <u>Stage 3 (2wk):</u> subjects assigned to either:	EE EI Appetite sensations Disinhibition	<u>Mean ExEE (kcal/session)</u> LI-Ex: 96 MI-Ex: 354 <u>Mean EI (kcal/d) during stage 3:</u> (kcal/d) — <u>Ex days</u> — <u>No-Ex days</u> LI-Ex — 1952 ± 87 — 1826 ± 131 HI-Ex — 1948 ± 81 — 1785 ± 122 No sig difference between EI on Ex and no-Ex days or between LI and HI.	ExEE did not sig effect EI in reduced obese women. Results suggest eating habits as opposed to physiological signals produced during Ex have a greater	EI measured by weighed intake of meals by investigators. Subjects recorded food intake at non-meal times Investigator was present during ad libitum feeding. May have effected EI

	± 1.5		1. LI-Ex (resistance weight training) 2. MI-Ex (aerobic) During stage 3, ad libitum feeding of food provided throughout the day (breakfast, lunch, dinner, and snacks). LI-Ex: Placebo. Resistance Ex to maintain strength only 5x30 min p/wk. MI-Ex: walking (75% VO_2max) 5 sessions/wk. Duration 29-55 min (EE: 20%RMR)		<u>%EI of Maintenance diet in stage 2:</u> LI-Ex: 101% HI-Ex: 98% No sig difference Division of subjects into over-eaters (n=7) and under-eaters (n=8) based on EI during stage 3: <u>Mean EI (kcal/d) during stage 3:</u> Over-eaters: 2536 ± 161 Under-eaters: 1353 ± 84 Sig difference in EI between over-eaters and under-eaters ($p<0.0001$) independent of ExEE. <u>%EI of Maintenance diet in stage 2:</u> Overeaters: 134 ± 6% Under-eaters: 72 ± 5% Sig difference ($p<0.0001$) Hunger and disinhibition ratings were sig and consistently higher in over-eaters ($p<0.02$, $p<0.004$ respectively), compared to under-eaters	influence on EI.	Over-eaters consumed sig higher % of fat in ad libitum diet (34%) than under-eaters (27%) ($p<0.0001$) Hunger, disinhibition, restraint were measured using the Eating Inventory administered 5 times throughout the 3 stages EI during Ex period ranged from 49-157% of maintenance EI BW loss of ~0.3kg in both groups during stage 3 BW and BC was measured by BIA
Broeder *et al.*, 1992	47 men Healthy, physically Active	12 wk ex intervention	Randomised Control Trial 1.Con 2.Resistance-	EE EI	<u>Mean ExEE (kcal/d):</u> ET: 650kcal/d RT: unknown <u>Mean EI</u>	Both RT and ET ExEE induced a slight decrease in EI, but this	EI measured through 3 day dietary record at wk 0, 6-7, 12

	Mean age (y): 18-35 Mean BMI (kg·m^{-2}): 25.3 ± 1.0 Mean BF (%): 20 ± 1.9		trained (RT) 3.Endurance-trained (ET) <u>RT</u>: 4d/wk, heavy resistance training Intensity gradually increased. <u>ET</u>: walk and/or jog 4d/wk. Intensity and duration gradually increased. w0-wk4: 0min (70%VO_2max) wk8-12: 50mins (70-90% VO_2max)		(kcal/d) <u>Pre-trial</u> <u>Post-trial</u> Con 2746 ± 214 2412 ± 191 RT 2603 ± 214 2412 ± 191 ET 2746 ± 191 2531 ± 238 No sig difference in EI between trials or compared to baseline No sig change in BW ET and RT sig reduced BF by 9.6% and 11.8% respectively No sig changes in body composition in Con	was not sig.	No sig changes in PA occured during trials RT: heavy resistance training incl. Bench press, tricpepressdown, leg press, leg curl, abdominal crunch BC was measured by hydrostatic weighing and skinfolds
Westerterp *et al.*, 1992	11 women 12 men Healthy Sedentary Mean age (y): 36 Mean BMI (kg·m^{-2}): 19.4-26.4	44 wk ex intervention	Training program to run half-marathon 4x Ex sessions p/wk for 44 wk, gradually increasing Ex time: Wk 8: 10-30mins Wk 20: 20-60mins Wk 40: 30-90mins	EE EI	<u>Median total EE</u> (kcal/d) <u>Men</u> <u>Women</u> Wk 0 2770±1242 2364±525 Wk 40 3463±812 2794±644 Sig increase in EE at wk 40 compared to baseline in both men ($P<0.01$) and women ($P<0.05$). <u>Median EI (kcal/d)</u> (kcal/d) <u>Men</u> <u>Women</u> Wk 0 2818±191 2173±1027 Wk 8 2818±1600 2149±1194 Wk 20 2698±1170 2077±1313 Wk 40 2436±1695 2269±1504	There was a significant increase in energy expenditure by week 40 in both men and women, but no sig difference in EI compared to baseline. Men tended to decrease EI leading to a	EI measured by 7 d dietary record BC was measured by hydrostatic weighing Total daily EE measured by DLW in 8 randomly selected subjects (2wk period). (Only 4 of these had EE measured at wk 8

					No sig difference in EI during training period in either men or women. In women EI was not sig higher from EE throughout study. In men EE was greater than EI causing negative EB in wk 8 ($p<0.05$), wk 20 ($p<0.05$) and wk 40 ($p<0.01$) Men tended to decrease EI from wk 20-40 and women tended to increase EI, but difference was not sig different from baseline in either sex Sig, but modest, reduction in BM in men ($p<0.01$), but not women FM was sig lower at wk 40 than baseline in both men ($p<0.001$) and women ($p<0.05$) as was FFM in men ($p<0.01$) and women ($p<0.05$)	state of negative EB. Women on the other hand tended to increase EI suggesting partial compensation.	and wk 20) In men, subjects with higher %BF lost more fat than those who were leaner at the start. This was not seen in women.
Staten, 1991	10 men 10 women Healthy, sedentary Mean BMI ($kg \cdot m^{-2}$): M: 68.3 ± 6.5, F: 56.7 ± 5.8 Mean BF (%): M: 11.6 ± 2.3, F: 25.7 ± 3.8	5 d ex intervention	Randomised cross-over design Each trial 5 d 1. Con 2. Ex, 1h/d treadmill running at 70% VO_2max Ad lib feeding of standardised food items in research	EE EI	<u>Mean ExEE</u> (not incl.RMR) (kcal/d): M: 596 F:382 <u>Mean EI</u> (kcal/d) <u>Men</u> <u>Women</u> Con 2467 ± 165 1831 ± 103 Ex 2685 ± 188 1830 ± 91 Sig increase in mean daily EI in men of 208 kcal/d ($p<0.02$) during the Ex trial, but no sig increase in EI in women	ExEE resulted in partial EI compensation in men but not women. As the increase in EI was insufficient to match ExEE both men and women were in negative	Subjects were blinded to main aim of study. EI measured through weighed intake by investigators. Food choice restrictive which may confound

	Mean VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$): M: 47.3 ± 6.2, F: 36.9 ± 6.0		centre for 5 d		% subjects increasing EI during Ex trial: M: 90% , F: 40%	energy balance during exercise trial.	results. No sig change in BW – due to small sample size, and short duration.
Woo and Pi-Sunyer, 1985	5 women Healthy, sedentary Body wt (kg): 54.8 ± 2.8	5 d evaluation phase and 3 19 d treatment periods	Effects of ex on EI of hospitalised normal-wt women 5 d evaluation: estimation of sedentary activity levels 19 d treatments: a. sedentary, b. mild (110% sedentary expenditure), c. (125% sedentary expenditure) Ex: treadmill walking, distributed throughout the day	TEE, EI BC, BW	Subjects maintained en equilibrium and stable BW and BC during all 3 treatments No sig difference in the time spent/cost of sedentary activities Mild / Moderate Ex time (mn/d): 139 / 250 ExEE (kcal/d): 378 ± 63 / 772 ± 40 EI (kcal/d): 2015 ± 88 / 2098 ± 96 EB (kcal/d): 64 ± 43 / -116 ± 92	Normal wt women increased their EI as EE increased up to EB levels	No compensation was observed in any of the treatments BC: EB + N balance, TBW + N balance EI : ad libitum buffet, weighted foods before and after consumption + bomb calorimetry nitrogen analysis EE: min to min activity diaries and indirect calorimetry
Woo and Pi-Sunyer, 1982a	6 women Healthy, sedentary Mean age (y): 42.6 ± 5.3	5 d evaluation phase and 3 19 d treatment periods	Effects of ex on EI of hospitalised O women 5 d evaluation: estimation of	EB: TEE, EI BC, BW	The total mean weight, fat, and LBM changes over 57 days were -2.30, -1.20, and -1.24 kg, respectively but none was sig	Obese women did not compensated by increasing their EI as EE increased.	Compensation occurred in non-exercise expenditure in both ex treatments

	Body wt (kg): 92.1 ± 5.5		sedentary activity levels 19 d treatments: a. sedentary, b. mild (109% sedentary expenditure), c. (122% sedentary expenditure) Ex: treadmill walking, distributed throughout the day		Mean daily intake was not different between the three treatments Mild / Moderate Ex time (mn/d): 39 / 96 ExEE (kcal/d): 281 / 694 EI (kcal/d): 2305 ± 163 / 2345 ± 196 EB (kcal/d): -114 / -369 although EE increased sig		All subjects responded to increased expenditure in a similar manner BC: EB+ N balance, TBW + N balance EI : ad libitum buffet, weighted foods before and after consumption + bomb calorimetry + nitrogen analysis EE: min to min activity diaries and indirect calorimetry
Woo et al., 1982b	3 women Healthy, Sedentary Mean age (y): 42.6 ± 5.3 Body wt (kg): 92.1 ± 5.5	5 d evaluation phase and 3 19 d treatment periods	Effects of exercise on energy intake of hospitalised obese women 5 d evaluation: estimation of sedentary activity levels 19 d treatments: a. sedentary, b.	EB: TEE, EI BC, BW	Mean daily intake (1903 kcal/day) and expenditure (2882 kcal/day) did not change with time. As a result, negative energy balance was obtained and sustained. A consistent rate of wt loss (0.12 kg/day) at a reasonable cost (8200 kcal/kg) occurred.	Therefore, obese women doing long-term moderate exercise do not compensate by an increase in caloric intake. This can produce a	BC: EB+ N balance, TBW + N balance EI : ad libitum buffet, weighted foods before and after consumption + bomb calorimetry + nitrogen analysis

			mild (109% sedentary expenditure), c. (122% sedentary expenditure) Ex: treadmill walking, distributed throughout the day			negative caloric balance when ex is coupled with ad libitum selection of ordinary foods.	EE: min to min activity diaries and indirect calorimetry

Abbreviations. AG, acylated ghrelin; Approx., approximately; BC, body composition; BF, body fat; BIA, bioelectrical impedance; BM, body mass; BMI, body mass index; BMR, basal metabolic rate; BP, blood pressure; BW, body weight; Con, control; DEXA, dual energy x-ray adsorptiometry; DLW, doubly labelled water; EB, energy balance; EE, energy expenditure; EI, energy intake; Ex, exercise; ExEE, exercise energy expenditure; F, females; FFQ, food frequency questionnaire; FFM, fat free mass; FM, fat mass; GLP-1, glucagon like peptide -1; H, high; HDL, high-density lipoprotein; HI-Ex, high-intensity exercise; HF, high fat; HR, heart rate; KKW, kcal/kg/week; LBM, lean body mass; LI-Ex, low intensity exercise; LF, low fat; max, maximum; LT, lactate threshold; M, males; M, moderate; MI, moderate-intensity; N, nitrogen; NEFA, non-esterified fatty acids; O, obese; OW, overweight; PA, physical activity; PAL, physical activity level; PYY, peptide YY; RMR, resting metabolic rate; SAEE, spontaneous activity energy expenditure; Sig, significant; SQ, satiety quotient; SMR, sleeping metabolic rate; TBW, total body mass; TEE, total energy expenditure; TG, triglycerides; VO_2, oxygen uptake; WC, waist circumference

1.5 Metabolic health benefits of physical activity

As previously mentioned, physical activity is not only considered a weight management aid, but also has the potential to offer multiple health benefits. This thesis attempts to investigate both physical and metabolic benefits of physical activity, therefore literature on the mechanisms by which physical activity is likely to affect chronic disease risk are briefly reviewed in this part.

Physical inactivity is an independent modifiable risk factor for CVD and other chronic diseases, including type 2 diabetes, cancer (colon and breast), obesity, hypertension, bone and joint diseases (osteoporosis and osteoarthritis), and depression (Warburton, 2006). In particular, there is strong evidence demonstrating that physical activity and fitness can reduce CVD and risk of type 2 diabetes by normalizing metabolic dysfunction particularly associated with features of the metabolic syndrome (Gill and Malkova, 2006). Data accumulated through cohort prospective, retrospective studies and controlled studies all agree that physical activity can attenuate several metabolic risk factors either independently and directly or through body fat reduction and/ or fitness increase (Gill and Malkova, 2006). Main physiological changes affected beneficially by physical activity seem to be interrelated and include changes in insulin sensitivity (Mayer-Davis et al., 1998; Wood et al., 1998), lipid and lipoprotein metabolism (Saris et al., 2003; Stefanick et al., 1998; Durstine et al., 2001; Leon and Santhez, 2001), endothelial function and inflammation (Gill and Malkova 2006; Sullivan et al., 2005; Whelton et al., 2002).

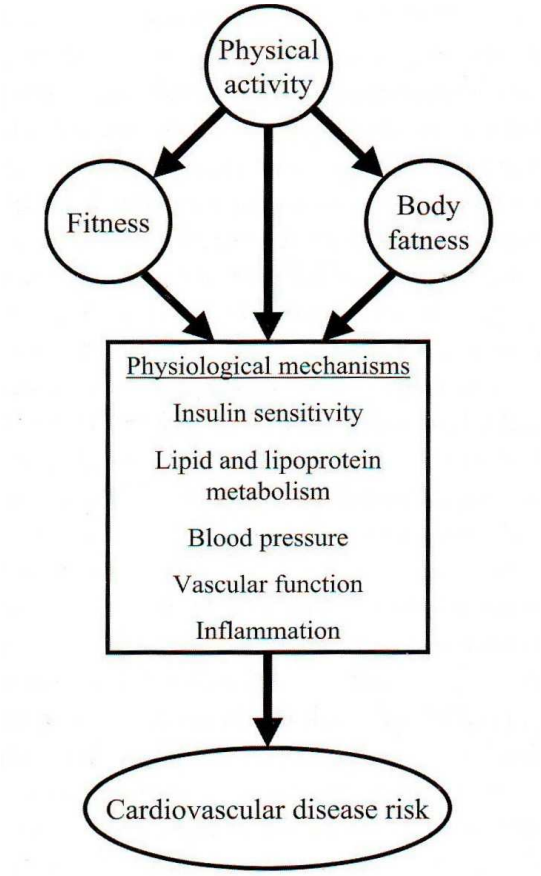


Figure 1.1 Mechanisms by which physical activity is likely to influence cardiovascular disease risk. Adapted from Gill and Malkova (2006).

1.5.1 Impact on insulin sensitivity and glucose tolerance

The term insulin sensitivity stands for the capacity of cells to respond to insulin-stimulated glucose uptake following ingestion of carbohydrates (Lebovitz and Banerji, 2005). Normal insulin function includes increased cellular glucose uptake, glycogen synthesis and suppression of hepatic glucose production (Petersen and Shulman, 2002). Insulin resistance on the other hand is a disorder, which denotes the inefficient insulin function in skeletal muscle, liver and adipocyte level (Holloszy, 2005; Haag and

Dippenaar, 2005). Insulin resistance is a central feature of the metabolic syndrome and acts independently but also synergistically with other factors to the development of CVD and type 2 diabetes (Benjamin et al., 2003; Reaven et al., 1999).

Insulin resistance is commonly increased in obesity (Haag and Dippenaar, 2005) and particularly in individuals with increased adiposity in the visceral compartment (Lebovitz and Banerji, 2005). Visceral adipocytes are metabolically more active than subcutaneous, merely because adipokines, produced by adipose tissue, have the ability to influence other tissues such as liver and skeletal muscle through the dynamic flux of fatty acids and tissue-derived hormones. Increased visceral fat impairs the activity of hormone sensitive lipase, which leads to enhanced lipolysis, release of non-esterified fatty acids (NEFA) and plasma NEFA concentration (Delarue and Magnan, 2007). This process induces chronic skeletal muscle insulin resistance through reduced carbohydrate oxidation and lower insulin stimulated glucose uptake (Boden and Shulman, 2002). In addition, increased amounts of NEFA increase gluconeogenesis in the liver (Roden et al., 2000) with concomitant decrease in hepatic insulin clearance and increased hepatic insulin resistance, which leads to hyperinsulinaemia and increased peripheral insulin resistance (Lebovitz and Banerji, 2005). Finally, under insulin resistant conditions hepatic triglyceride (TG) synthesis and secretion of very low density lipoprotein (VLDL) are very elevated (Haag and Dippenaar, 2005). Subsequently a vicious cycle is introduced where impaired insulin function fails to suppress lipolysis, producing further lipid overflow to the liver and skeletal muscle and finally leading to increased insulin resistance (Rosenberg et al., 2005; Haag and Dippenaar, 2005). Sedentary, obese and

insulin resistant individuals apart from reduced lipid turnover are also reported to have impaired mitochondrial efficiency and as such, the amount of free fatty acids (FFA) to enter the mitochondrial matrix increases. Free fatty acids are then prone to lipid peroxidation and highly reactive cytotoxic metabolites that damage DNA and proteins are produced, a fact which further hinders mitochondrial oxidative capacity and increases insulin resistance (Ho et al., 2002).

Although inconsistent, the literature shows that acute exercise leads to enhancements of insulin-mediated glucose metabolism and insulin sensitivity in healthy individuals (Nassis et al., 2009, Kim et al., 2007; Henriksen et al., 2007; Nassis et al., 2005; Hasbum et al., 2005; Duncan et al., 2003; Zierath et al., 2002; Dengel et al., 1996). The mechanisms by which physical activity may affect insulin sensitivity are not yet fully elucidated, however, it is recognised they are partly mediated by reduction in adiposity and central obesity (Schenk et al., 2009; Johnson et al., 2009; Bo et al., 2008; Kim et al., 2007; Goodpaster et al., 1999; Rice et al., 1999). However, in overweight and obese individuals, insulin sensitivity improves not only through the synergistic effect of exercise and weight loss but also through weight loss- independent mechanisms (Nassis et al., 2009, Nassis et al., 2005; Duncan et al., 2003; Dengel et al., 1996). For example, Nassis et al (2009; 2005) showed that insulin sensitivity measured by oral glucose tolerance test improved by 23.3% after a 12-week exercise programme in overweight and obese girls. This occurred without changes in body mass, body fat, waist circumference and inflammatory markers. Similarly, Duncan et al., (2003) demonstrated that 6 months of walking exercise increased insulin sensitivity in sedentary adults

without weight loss. Another study examined the independent and combined effects of aerobic exercise training and weight loss on glucose metabolism in 47 obese sedentary older men over 10 months (Dengel et al., 1996). It was found all combinations improved insulin sensitivity but through different mechanisms. Insulin sensitivity improvement through exercise, therefore, is rather attributed to altered function of adipose tissue, contrary to cosmetic methods that decrease body fat but not its metabolic function (Mohammed et al., 2008; Klein et al., 2004).

It is well established that the beneficial effect exercise is able to induce on insulin sensitivity is mainly attributable to increased metabolic activity in the skeletal muscle level (Gill and Malkova, 2006). Insulin sensitivity and responsiveness, measured by euglycaemic- hyperinsulinemic clamp, has been shown to improve following a single exercise session for up to 48 hours (Turcotte and Fischer, 2008). Magkos et al., 2010 suggested that insulin sensitivity assessed by homeostasis model increased 12 hours after a single bout of moderate-intensity endurance exercise in a normogycaemic population. Similarly, acute exercise improved insulin resistance and glucose tolerance in type 2 diabetes patients (Bordenave et al., 2008) and older individuals with impaired glucose tolerance (Bloem and Chang, 2008). Improvements in insulin sensitivity following a single exercise bout are thought to be mediated by mechanisms of insulin-dependent and insulin-independent stimulation of GLUT-4 translocation and expression to the cell surface and subsequent increased glucose uptake by the myocyte (Gill and Malkova 2006; Long et al., 2004; Zierath, 2002). These mechanisms are closely dependent to contractile ability of the muscle and acute exercise-induced energy deficit (Eriksen et al.,

2007; Wright et al., 2006; Holloszy, 2005), as these appear to be normal in insulin resistant (Brozinick et al., 1994; Brozinick et al., 1992) or in type 2 diabetic individuals (Kennedy et al., 1999; Azevedo et al., 1995) independently of enhanced insulin signalling. However, acute changes in insulin sensitivity following an exercise session do not persist longer than 48 hours (Turcotte and Fischer, 2008).

Endurance exercise training has been shown to enhance insulin sensitivity in healthy populations (Nassis et al., 2009, 2005; Kim et al., 2007; Di Pietro et al., 2006; Houmard et al., 2004; Duncan et al., 2001; Dengel et al., 1996) as well as in insulin resistant individuals (Kelley and Goodpaster, 1999) and improve glucose tolerance in insulin resistant populations (Saengsirisuwan et al., 2001; Steen et al., 1999; Hevener et al., 2000; Eriksson et al., 1998; Perseghin et al., 1996). Furthermore, few studies suggest that insulin-resistant offspring of type 2 diabetic patients were more beneficially influenced by exercise than healthy controls and as such, the effect of physical activity on insulin sensitivity is more profound in insulin resistant individuals (Barwell et al., 2008; Perseghin et al., 1997). Additionally, it is shown that although physical activity encompasses a wide range of intensity and volume that act beneficially on insulin resistance, it seems that there exists a dose-dependent response (Di Pietro et al., 2006; Houmard et al., 2004). Repeated bouts of exercise and regular exercise may potentiate the effects of exercise on insulin sensitivity through multiple adaptations in glucose transport and metabolism (Borghouts and Keizer, 2000). Mechanisms leading to these changes are related to increased oxidative capacity of the muscle, skeletal muscle vascularity and insulin-dependent and independent stimulation of GLUT-4 cycling

(Colberg and Grieco, 2009). In addition, training may elicit favourable changes in lipid metabolism and is able to bring about improvements in the regulation of hepatic glucose output (Borghouts and Keizer, 2000). Exercise increases free fatty acid (FFA) oxidation, which subsequently are diverted from producing damaging lipid intermediates such as long chain acyl CoA, ceramide and diacylglycerol that can inhibit insulin action (Turcotte and Fischer, 2008; Schenk and Horowitz, 2007; Wojtaszewski and Richter, 2006; Bruce et al., 2006). This occurs apparently through the enhanced mitochondrial quality, quantity and oxidative ability of the muscle triggered by exercise (Menshikova et al., 2005). Enhanced activity of mitochondrial oxidative enzymes such as citrate synthase and β-hydroxyacyl CoA dehydrogenase (β-HAD) by exercise (Hansen et al., 2005) are reported to be strong predictors of insulin sensitivity (Bruce et al., 2003). In parallel, substrate availability and muscle glycogen depletion seem to be related to these responses (Hansen et al., 2005; Holloszy, 2005; Wojtaszewski et al., 2003). Moreover, reductions in lipid metabolite concentrations may partly explain the improvements in GLUT-4 translocation and activities of enzymes as hexokinase and glycogen synthase (Horowitz, 2007; Holloszy, 2005; Wasserman and Ayala, 2005; Crist-Roberts and Mandarino, 2004). Increased insulin sensitivity has been also shown to be interrelated to reduced circulating leptin following energy deficit induced by an exercise intervention (Essig et al., 2000). Reduced leptin concentrations are thought to enhance insulin sensitivity in synergy with increased fat oxidation stimulated by exercise (Solomon et al., 2008). Additionally, the anti-inflammatory effects of exercise; reducing markers of low grade inflammation; may also increase GLUT-4 expression (Kadoglou et al., 2007; Petersen and Pedersen, 2005). The beneficial effects on insulin sensitivity may persist

for a few days and then disappear (Shojaee-Moradie et al., 2006), which lends support to the current public health recommendations stating that exercise should be performed regularly or on most days of the week (Haskell et al., 2007). Conclusively, it seems that chronic adaptive responses to exercise mediated by acute changes are likely to increase insulin sensitivity, especially in insulin resistant, other 'at risk' populations and individuals who lose weight. It still remains unclear how different exercise characteristics such as frequency and duration of an individual session may affect insulin sensitivity in different populations.

1.5.2 Impact on lipids and lipoproteins

Dyslipidaemia is an important, potentially reversible risk factor for CVD (Cunnane and Griffin, 2002). The atherogenic profile could be mainly described as a compilation of factors such as elevated low-density lipoprotein (LDL)- especially small dense LDL_3 concentration, low levels of high-density lipoprotein (HDL), and high levels of TG (Austin et al., 1990) and is considered to play a major role in pathogenesis of atherosclerosis (Cohn , 1998).

It is widely accepted that long term exercise exerts benefits to lipoprotein profile of individuals even in the absence of weight loss (Linna et al., 2007; Pedersen and Saltin 2006; Barengo et al., 2006; Kelley et al., 2005) with exercise mode intensity and duration being important predictors of disease risk (Kraus et al., 2009; Duscha et al., 2005; Kraus et al., 2002). Specifically, exercise is known to reduce TG concentrations, to increase HDL levels, and controversy persists whether it is also beneficial in changing

other components such as total and LDL-cholesterol (Leon and Santchez, 2006). In addition to these main effects, it has been demonstrated that increasing physical activity may induce changes in other potential factors of the atherogenic lipoprotein profile, such as a shift in lipoprotein subclass distribution, increasing the mean size of HDL and LDL particles (Kraus et al., 2002). However, beneficial lipid alterations do not always occur following exercise programmes (Despres et al., 1994; Durstine et al., 1994). These findings could potentially be explained by clinically normal level of pre-trial lipids, interindividual differences in subjects, pre-training concentrations, diet, weight loss, altered body composition, training volume and intensity or even timing of blood collection (Kraus and Slentz, 2009). For example, it is shown that lipids concentration improves favourably mainly in those individuals with the poorest baseline lipid profile (Church et al., 2007; Haskell et al., 1986) or the effect attributed to a whole exercise programme may reflect mainly the effect of the last single exercise session on lipid metabolism (Crouse et al., 1997). It is widely accepted, that the favourable lipoprotein lipid profile evident in regular exercisers is likely to be mainly a consequence of the repeated acute effect of single exercise sessions. The main lipid change following a single exercise session is decreased TG concentration (Gill, 2004; Hardman et al., 1998) and it is suggested that the level of the effect is related to the ExEE rather than exercise intensity (Gill and Hardman, 2003). The effect of acute exercise on lipid metabolism is likely to be mediated by the increased action of lipoprotein lipase (LPL), which increases clearance of TG into exercised skeletal muscle, and the reduced hepatic production of VLDL (Gill and Malkova, 2006).

It is suggested, that as humans spend most of their time in the postprandial state, this state is highly associated with several atherogenic risk factors and the pathogenesis of atherosclerosis (Petitt and Cureton, 2003). Postprandial lipaemia – a term describing lipid and lipoprotein metabolism following food consumption – is claimed to be an independent cardiovascular disease risk factor even after controlling for fasting TG levels (Hyson et al., 2003; Patsch et al., 2000; Patsch et al., 1992). As a consequence, repeated episodes of exaggerated postprandial metabolism have the potential to create a recurring atherogenic environment (Malkova and Gill, 2006). There are several proposed mechanisms through which postprandial lipemia exerts its atherogenic effects. High postprandial concentrations of TG-rich lipoproteins are the primary driver of the atherogenic lipoprotein phenotype (Malkova and Gill, 2006). Postprandial lipoproteins and their remnants may deposit directly into the arterial wall, where they become oxidised and incorporate into atheromas (Funada et al., 2002; Cohn, 1998; Doi et al., 1998; Zilversmit, 1995). High postprandial triglyceride concentrations exert an atherogenic influence on other lipoproteins especially LDL and HDL, contributing to an "atherogenic lipoprotein phenotype" when the postprandial lipaemia is induced consistently by the regular ingestion of high-fat meals (Zilversmit, 1995). Other ominous changes are apparent in parallel, such as increase in pro-thrombotic and pro-inflammatory markers (Lanes et al., 2004; van Oostrom et al., 2004a,b; Gill et al., 2003) and impaired endothelial function (Harrison et al., 2004; Funada et al., 2002; Jagla and Schrezenmeir, 2001; Bae et al., 2001; Plotnick et al., 1997; Vogel et al., 1997).

Exercise is a potent regulator of postprandial lipid metabolism. The mechanisms responsible for the exercise related attenuation of postprandial TG are not fully understood. The lower postprandial TG concentrations after exercise may reflect an enhanced removal rate of TG-rich lipoproteins by peripheral tissues as LPL activity is upregulated after exercise in a time-course consistent with the postprandial reduction of TG (Zhang et al., 2004; Zhang et al., 1998; Seip et al., 1997). A decreased rate of VLDL synthesis and secretion from the liver is also a contributing factor and accounts, at least in part, for the remaining reduction in circulating postprandial TG (Gill and Hardman, 2003). However, these changes seem to be mediated by the acute effect of exercise on lipaemia rather than by a long-term training effect. Evidence from detraining studies indicate that postprandial TG concentrations rise by approximately 40-50% within a week of no training in endurance athletes or fit individuals and this increase is mostly evident within 60 hours after the end of the last exercise session (Gill et al., 2003; Herd et al., 1998; Hardman et al., 1998). In addition, a study comparing the effects of an acute exercise session with three consecutive sessions of the same ExEE per se, found that the TG-lowering effect of exercise is not augmented by exercising on repeated days (Farah et al., 2010). The influence of exercise intensity and substrate utilisation during exercise on the subsequent attenuation of postprandial TG appears to be of relatively less importance than TEE (Petitt and Cureton, 2003; Malkova et al., 1999; Tsetsonis and Hardman, 1996). For this reason, intermittent bouts of moderate-intensity exercise have been shown equally effective as continuous moderate-intensity exercise, provided the TEE is similar (Altena et al., 2004; Gill et al., 1998), however, the effect of other exercise characteristics such as frequency and session duration on postprandial lipaemia

has not been yet elucidated. Recently it has been proposed that the postprandial TG reduction observed following acute exercise can be replicated when overweight/obese male participants are fed *ad libitum* in a laboratory condition (Farah et al., 2010), but this was not confirmed in lean male individuals (King et al., 2010a,b). Still, the impact of *ad libitum* feeding which resembles a "real-life" situation, on female post-exercise lipaemic responses remains unclear.

1.5.3 Impact on inflammation

Chronic disease such as type 2 diabetes and atherosclerosis are associated with low-grade chronic inflammation (Lee and Pratley, 2007; Ross, 1999), which is reflected by increased C-reactive protein (CRP) concentrations and increased cytokines with immunoregulatory properties such as tumor necrosis factor- α (TNF-α), and interleukins (IL-1β, IL-6, IL-1) (Duncan et al., 2003; Festa et al., 2002; Ford et al., 2002; Freeman et al., 2002; Wallenius et al., 2002). According to research evidence, physical exercise has anti-inflammatory properties and therefore is expected to protect against chronic disease acting either through body fatness reduction or independently (Petersen and Pedersen, 2005).

In the short-term it is anticipated that strenuous exercise produces a transient increase in inflammatory markers such as TNF-α and CRP (Kasapis and Thompson, 2005). A study looking at the inflammatory responses in athletes showed that CRP increased by 266%, 24 hours after a prolonged race and returned to baseline 48 hours later (Taylor et al., 1987). This acute response to exercise seems to be proportional to the amount of activity

and muscle injury (Kasapis and Thompson, 2005). However, acute exercise is also shown to produce an increase in various anti-inflammatory mediators, (Febbraio and Pedersen, 2002; Ostrowski et al., 2001; Ostrowski et al., 1999; Ostrowski et al., 1998; Jordan et al., 1997). Interestingly, TNF-α response was attenuated in people injected with *Escherichia coli* endotoxin after a single exercise session (Starkie et al., 2001). The finding that exercise suppresses TNF-α production was supported by another study demonstrating that exercise normalises overexpression of TNF-α in TNF receptor knockout mice (Keller et al., 2004). One mechanism accounting for this parallel protective effect of exercise, is the high circulating levels of IL-6 and its anti-inflammatory properties (Streensberg et al., 2003) such as inhibition of TNF-α production, (Matthys et al., 2000). In addition, it is possible that exercise is likely to suppress inflammatory indices also via IL-6-independent pathways, as demonstrated by the finding of a modest decrease of TNF-α after exercise in IL-6 knockout mice (Keller et al., 2004); maybe through increased levels of epinephrine (Van der Poll et al., 1996).

It is hypothesised, that regular exercise amplifies the anti-inflammatory effects of an acute exercise bout of exercise and therefore is able to protect against chronic systemic low-grade inflammation over the long term, but such a hypothesis is not yet proven (Petersen and Pedersen, 2005). Cross-sectional studies demonstrated an association between physical inactivity and low-grade systemic inflammation in healthy subjects (King et al. 2003; Geffken et al., 2001; Smith et al., 1999). A review of the impact of lifestyle interventions on systemic inflammation shows an inverse relationship between exercise/ fitness and markers of inflammation after controlling for BMI or other

measures of adiposity (Nicklas et al., 2005). Findings from longitudinal studies, however, are contradictory with some indicating that regular training induces a reduction in inflammatory markers (Fallon et al., 2001; Smith et al., 1999) and others showing no effect (Fredrikson et al., 2004; Rawson et al., 2003).

Nine months of endurance exercise in preparation for running a marathon significantly reduced CRP levels in 10 runners compared with non exercise controls (Mattusch et al., 2000). In contrast, Thompson et al., (2010) found that IL-6 decreased during the course of a 24-weeks moderate exercise intervention, but this effect disappeared within 2 weeks of detraining while other inflammatory markers as CRP did not change significantly. The biggest study so far- the HERITAGE Family Study- found that a 20-week exercise intervention did not reduce CRP levels in the group as a whole but significantly reduced CRP to those with higher initial levels (Lakka et al., 2005). Many of these results could also be explained by gender differences. Indeed, a recent study indicates that although women have a better atherogenic profile at baseline, they have significantly higher levels of CRP than men (Garelnabi et al., 2010). The mechanisms behind the anti-inflammatory effect of regular exercise have not been fully elucidated and may be partly related to fat loss but as it is aforementioned this is not always the case. Other suggested mechanisms contributing to the anti-inflammatory effects of exercise training apart from the increases in production of anti-inflammatory cytokines, include increased antioxidant capacity in skeletal muscle (Gill and Malkova, 2006).

1.5.4 Impact on endothelial function

Endothelial function describes the ability of the endothelium of the blood vessels to interact with vascular smooth muscle to influence blood flow (Cines et al., 1998). The endothelium is considered an active organ with many physical and chemical properties and main responsibility to keep vascular-tissue homeostasis by modulating vasodilation and vasoconstriction, controlling production of prothrombotic and antithrombotic components, and fibrynolitics and antifibrynolitics and intervening in immunological processes (Landmesser et al., 2004; Libby et al., 2002; Moncada et al., 2001)

There is accumulating evidence that endothelial dysfunction represents one of the earliest events in the pathogenesis of cardiovascular disease and is currently considered an independent atherosclerotic disease risk factor (Moyna and Thompson, 2004; Moyna et al., 2001; Sorenson et al., 2001). Endothelial dysfunction is characterized in part by increased levels of chronic systemic low-grade inflammation (Pearson et al., 2003), impairment of atheroprotective substances such as nitric oxide (NO) and soluble isoforms of adhesion molecules such as intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) (Meydani, 2003; Hope and Meradith, 2003; Davies et al., 1993). The appearance of soluble cell adhesion molecules in the circulation likely reflects endothelial inflammation/ activation and an increase in their expression on the cell surface (Meydani, 2003; Leeuwenberg et al., 1992).

Acute exercise induces increases in shear stress, blood flow and regulation of blood pressure, which have a positive effect on endothelial function (Niebauer and Cooke, 1996). A number of factors may contribute to this event. For example shear stress

produced by exercise is a potent stimulus for NO release, which enhances the endothelium-dependent vasodilation of coronary arteries (Niebauer and Cooke, 1996). The effect of exercise on the number and function of endothelial progenitor cells, which represent an important endogenous repair mechanism, is also likely to contribute to the improvement in endothelial function observed in response to exercise (Hoetzer et al., 2007; Rehman and Parvathaneni, 2004).

The repetitive increases in coronary and peripheral blood flow in response to regular exercise may facilitate coronary artery adaptations that enhance the endothelial response to shear stress. However, studies examining exercise training on endothelial function on healthy volunteers are quite contradictory with some of them indicating an improvement (Clarkson et al., 1999; Higashi et al., 1999) and others demonstrating no effect (Kingwell et al., 1997; Green et al., 1994). It is evident nevertheless, that endothelial response to exercise training in humans depends largely on baseline levels of endothelial function (Moyna and Thompson, 2004). Improved endothelial function occurs in individuals with existing dysfunction at baseline such as the elderly, asymptomatic individuals with one or more CVD disease risk factors, and patients with CVD (Xiang and Wang, 2004; Kobayashi et al., 2003; Schmidt et al., 2002; Higashi et al., 1999; Hambrecht et al., 1998) but only rarely has exercise training improved endothelial function in healthy, young subjects (Altena et al., 2004; Clarkson et al., 1999).

1.6 Hypotheses and aims

The hypotheses of the studies contained within this thesis are as follows:

1) Participation in an exercise session with EE of 2 MJ, which corresponds to recommended ExEE required to reduce body weight does not lead to compensatory increase in appetite and energy intake when observed over 24 hours and favourably modifies markers of metabolic health measured in response to *ad libitum* meals, which resemble "real-life" eating conditions.

2) There is intra-individual variability in relation to exercise induced body fat and body mass loss with some but not all individuals compensating for exercise induced energy balance by increasing energy intake and reducing activity outside exercise sessions.

3) Recommended physical activity level and subsequent benefits can be achieved not only by exercising at moderate-intensity for 30 minutes on five days of the week but also by exercising at moderate-intensity less frequently but for longer duration.

Therefore aims of this thesis are:

1) To investigate the impact of a single moderate-intensity exercise session with EE of 2 MJ on appetite measures, energy intake and metabolic variables in response to four *ad libitum* meals in overweight females (Chapter 3).

2) To examine the extent to which changes in physical activity outside of the exercise intervention and energy intake contribute to individual differences in body fat loss induced by exercise training programmes (Chapter 4).

3) To investigate how health characteristics of overweight middle aged women are influenced by 8-week supervised aerobic exercise programmes with exercise sessions conducted twice per week for the duration of 75 minutes and exercise sessions conducted 5 times per week for the duration of 30 minutes (Chapter 5).

Chapter 2: General Methods

2.1 Participants recruitment and ethical approvals

Ethical approvals for all studies were obtained by University of Glasgow, Faculty of Biomedical and Life Sciences, Ethics Committee for non-clinical research involving human subjects, material or data. Participants were recruited via an advertisement in the University newsletter, posters (Appendix Ia,b), e-mails and a study website. Posters were located in Royal Hospital for Sick Children, Western Infirmary Hospital, Royal Infirmary Hospital and in the Glasgow University campus. When a volunteer contacted the researcher expressing an interest in taking part in a study, procedures were explained via telephone, e-mail or in person and they also received an information leaflet (Appendix IIa,b) to take away and make their decision. If the individual decided to take part in the study, she was asked to sign a consent form (Appendix IIIa,b), to complete a health screen form (Appendix IV) as well as an International Physical Activity Questionnaire (IPAQ) (Appendix V) so as to ensure that she was leading a sedentary lifestyle for at least one year. The volunteers personal information (contact phone numbers, e-mail, address) were only stored on a University of Glasgow computer server.

To be eligible for inclusion in all studies participants were required to be female, aged 18-45 years, in generally good health, overweight or obese with BMI between 25-35 $kg \cdot m^{-2}$ and sedentary (less than 1 h of planned exercise per week and physically inactive job). All participants were also non-smokers, not on weight reducing diet (weight stable for 1 month prior to testing was established with a questionnaire), not pregnant, had

regular menstrual cycle, blood pressure less than 160/90 mmHg and had not established CHD (for example myocardial infarction, stroke) or diabetes. Participants were required not to take any medication known to influence lipid or carbohydrate metabolism and any nutritional supplements or follow a special diet.

2.2 Anthropometry and physiological measurements

2.2.1 Height and weight

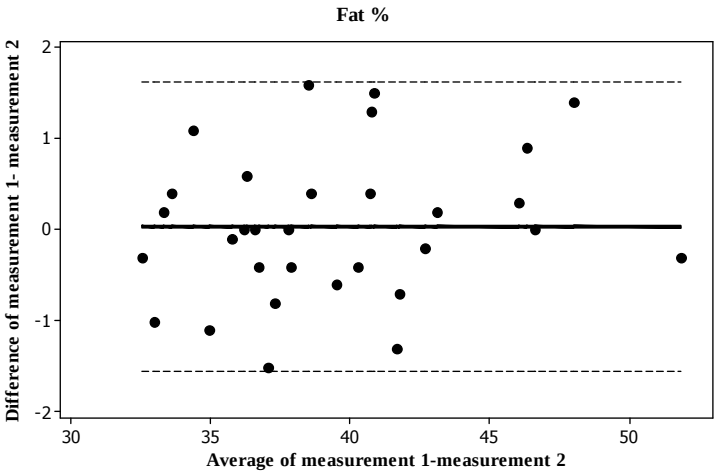
Height was measured using a portable stadiometer (Seca, Leicester, UK). Volunteers were measured barefoot, with their back positioned against a fixed backboard and their arms relaxed in the lateral position. The head was also positioned against the backboard, with the line of eyesight perpendicular to the backboard. Measurement was performed when the volunteer was positioned and relaxed, and a moveable headboard was lowered on to the top of the head with light pressure allowing hair compression. The investigator applied gentle upwards pressure underneath the angle of the mandible and measurement was made to the nearest 0.01 m.

Body mass was measured through digital scales (TBF-300, TANITA, Cranlea, UK). The same scale was used for all volunteers throughout the study. Subjects were weighed wearing lightweight clothing and without wearing shoes. Extraneous jewellery and clothing was removed prior to weighing. Body mass was measured with both feet flat on the balance and with arms positioned in the lateral position. Measurement was made to 0.05 kg. In order to calculate BMI, the derived values for height and weight measurements were used (Marfell-Jones, 2006).

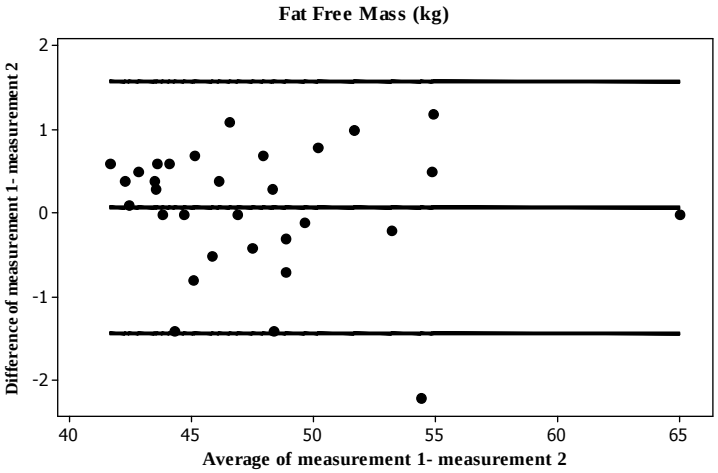
2.2.2 Body Composition

Components of body mass-body fat and fat free mass- were measured through leg-to-leg bioelectrical impedance analysis (TBF-300, TANITA, Cranlea, UK). Tanita scales determine the electrical impedance, or opposition to the flow of an electric current on body tissues, which can be used to calculate an estimate of total body water. Total body water then can be used to estimate fat-free body mass and, by difference with body weight, body fat. In this system, two footpad electrodes (pressure contact) are incorporated into the platform of a precision electronic scale. A person's measurements were taken while in a standing position with the electrodes in contact with bare feet. Bioelectrical impedance similarly estimates changes in the fat mass over a weight loss programme when compared to gold standard reference methods (Utter et al., 1999; Minderico et al., 2008). In order to determine the test-retest reliability of body composition measurements in this thesis, body composition was measured in 30 overweight and obese women on two occasions, at an interval of 2 days, using the bioelectrical impedance scales (TBF-300, TANITA, Cranlea, UK). The mean ± SD difference in fat mass between measurements was 0.05 ± 0.68 kg (0.16 ± 2.12%) and the mean ± SD difference in fat free mass was 0.07 ± 0.77 kg (0.14 ± 1.61%). Bland Altman analysis (Figure 2.1) revealed that the average bias is close to zero and there is no statistical difference between the two measurements, no side effects and good agreement, however there is a big variance.

A.


Fat %
Difference of measurement 1- measurement 2
Average of measurement 1-measurement 2
2
1
0
-1
-2
30
35
40
45
50

B.


Fat Free Mass (kg)
Difference of measurement 1- measurement 2
Average of measurement 1- measurement 2
2
1
0
-1
-2
40
45
50
55
60
65

C.

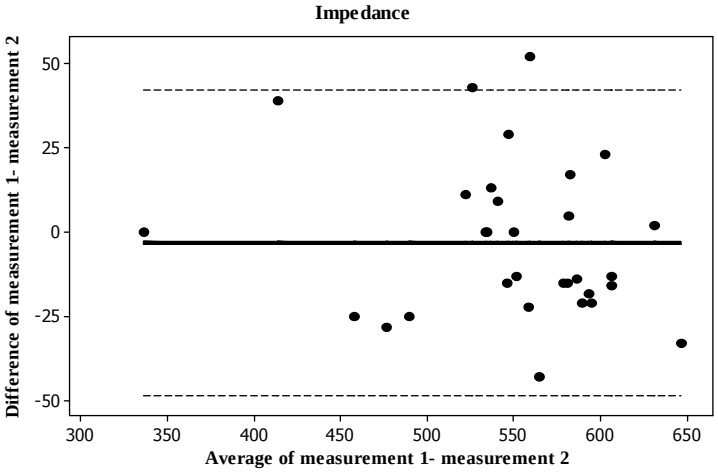

Impedance
Difference of measurement 1- measurement 2
Average of measurement 1- measurement 2
50
25
0
-25
-50
300
350
400
450
500
550
600
650

Figure 2.1 Bland Altman plots between difference of measurement 1- measurement 2 and average of measurement 1- measurement 2 for Fat% (A), Fat Free Mass (kg) (B) and Impedance (C).

2.2.3 Resting metabolic rate

Resting metabolic rate was measured in the metabolic investigation suite of West Medical Building in the University of Glasgow (Figure 2.2) in the morning after 12 hours fast and 24 hours abstention from exercise in a thermoneutral environment (21-24°C) using a ventilated hood system (Deltatrac, Datex Instrumentation Corporation, Helsinki, Finland) or an online system (Oxycon Pro, Jaeger GmbH, Hoechberg, Germany). Participants were asked to drive to the laboratory and where possible to minimise movement. On arrival at the laboratory volunteers were escorted to a quiet, semi-darkened room where they lie quietly for 10 minutes before measurement began with their arms at their sides and their legs straight and uncrossed, on the examination bed. A ventilated hood was then placed over the volunteer's head to allow analysis of expired gas. The individual was monitored throughout to ensure that sleeping, talking and excess movement did not occur. Background noise was kept minimum throughout the measurement. After 10 minutes supine rest, measurements of oxygen uptake ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) were made every 60 seconds for the duration of 30 minutes and RMR was calculated using indirect calorimetry equations described by Frayn and Macdonald, (1997):

$$\text{Rate of fat oxidation } (g \cdot min^{-1}) = (\dot{V}O_2 - \dot{V}CO_2)/0.57$$

Rate of carbohydrate oxidation ($g \cdot min^{-1}$) = (1.40 x $\dot{V}CO_2$ – $\dot{V}O_2$)/0.30

Rate of energy expenditure ($kJ \cdot min^{-1}$) = [rate of carbohydrate oxidation x 15.6] + [rate of fat oxidation x 39]

For each measurement the first 10 minutes were excluded, to ensure steady state values were used. Respiratory quotient values were automatically calculated by the equipment. Values were then averaged to obtain mean RMR and RQ values.

Figure 2.2 Metabolic Investigation Suite, West Medical Building, University of Glasgow

2.2.4 Blood pressure

Blood pressure was measured under controlled conditions and supine positioning, conforming to the European Society of Hypertension guidelines on blood pressure measurement (Parati et al., 2008). An automated monitor was used (Omron Healthcare

UK Limited, Milton Keynes, UK), and the lowest value of three readings was taken as the recorded value.

2.3 Cardiorespiratory fitness assessment

2.3.1 Submaximal exercise testing

Before participation in exercise testing each volunteer was asked to undertake a familiarisation session in order to be comfortable with the equipment. For the determination of maximal oxygen uptake $\dot{V}O_{2max}$ participants exercised on a cycle ergometer (Ergomedic 873, Monark, Sweden) at gradually increasing intensities starting at 50W with a graded increase of 15W every 5 minutes. Cycling cadence of 60 rpm was kept constant throughout the test. Heart rate was continuously recorded by short-range telemetry (Polar S610i, Polar Electro Oy, Kempele, Finland). At the end of each 5-minute stage, rate of perceived exertion (RPE) was indicated by the volunteer on the Borg scale (Borg and Noble, 1974) and an 1-minute expired air sample was collected in Douglas bags and immediately analysed through a gas analyser (Servomex 4000 series, Servomex Group Limited, East Sussex, UK). The test was terminated once the subject reached 85% of their age-predicted maximum HR (HR_{max}), which was determined by the formula (Fox and Haskell, 1968):

$$HR_{max} = 220 - age.$$

2.3.2 Expired air collection and analysis

Expired air was collected in Douglas bags, using the standard Douglas bag technique (Consolazio, 1963). Analysis of expired air was performed in two stages:

Stage 1: 0.5 litres of air were extracted through the sampling port of the Douglas bag at a constant flow rate, controlled by a flow meter. This air was passed into a gas analyser (Servomex 4000 series, Servomex Group Limited, East Sussex, UK) and the percentage fraction of O_2 and CO_2 were measured.

Stage 2: The remaining air was extracted by a vacuum at a constant flow rate, through a dry gas meter (Harvard Apparatus Ltd, Kent, UK) which provided a measurement of the volume of expired gas, and through the dry gas meter's thermometer, provided a measurement of the temperature of the expired air.

Prior to all tests, the gas analyser was calibrated against known reference gases (BOC Gases, BOC Limited, Surrey, UK) and barometric pressure was measured. All gas measurements were corrected to standard room temperature and pressure (STPD) for a dry gas. Values of $\dot{V}O_2$ and $\dot{V}CO_2$ were calculated from expired air using the Haldane transformation of the Fick equation as shown in equations below (Wilmore and Costill 1973):

$$\dot{V}I = \dot{V}E_{STPD} \text{ x } (100 - \text{Exp. Fraction } O_2 - \text{Exp. Fraction } CO_2) / 79.04$$

$$\dot{V}O_2 \ (l \cdot min^{-1}) = \dot{V}I \text{ x } 0.2093 - (\dot{V}E_{STPD} \text{ x Exp. Fraction } O_2 / 100)$$

$$\dot{V}CO_2 \ (l \cdot min^{-1}) = (\dot{V}E_{STPD} \text{ x Exp. Fraction } CO_2 / 100) - \dot{V}I \text{ x } 0.0003,$$

where $\dot{V}I$ = Volume inhaled, $\dot{V}E$= Volume exhaled

2.3.3 Prediction of $\dot{V}O_{2max}$

Mean HR was plotted against calculated $\dot{V}O_2$ for each stage of the submaximal exercise test. In all cases a linear relationship was observed between HR and $\dot{V}O_2$. $\dot{V}O_{2max}$ was predicted by extrapolation of the HR against $\dot{V}O_2$ plot to age-predicted HR_{max} (American College of Sports Medicine 1995).

2.3.4 Collection and preparation of samples for lactate measurements

A finger prick capillary blood sample was taken in the resting state, prior to the test, and in the last minute of each exercise testing stage. The initial resting sample was taken after the volunteer's left hand had been immersed for ten minutes in a bath of water heated to 42°C, to ensure increased blood flow and arterialisation of the sample. The thumb was swabbed with an alcohol wipe and prick was performed by digital puncture, using Accu-Chek Softclix lancets (Roche Diagnostics, Welwyn Garden City, UK). The initial blood droplet was wiped away, and then a 20 µl capillary blood sample was collected into 20 µl disposable glass capillary tubes (Fisher Scientific, Blaubrand tubes). The sample was immediately deproteinised by addition to 200 µl of ice-cold 0.4 mmol/l perchloric acid and the precipitate was separated by centrifugation at approximately 12.000 x g for 30 seconds (Eppendorf centrifuge, Eppendorf AG, Germany). The clear supernatant was then divided in duplicate eppendorfs and stored at -80°C until analysis for the determination of lactate threshold (LT) (Spurway, 1992).

2.4 Blood analysis

2.4.1 Insulin and soluble vascular cell adhesion molecule-1 measurements

In order to determine insulin levels, all samples were measured by a commercially available enzyme–linked immunoassay (ELISA) with <0.01% cross-reactivity with pro-insulin (Mercodia AB, Uppsala, Sweden). In principle, Mercodia Insulin ELISA is a solid phase two-site enzyme immunoassay. It is based on the direct "sandwich" technique in which two monoclonal antibodies are directed against separate antigenic determinants on the insulin molecule. During incubation insulin in the sample reacts with peroxidase- conjugated anti-insulin antibodies and anti-insulin antibodies bound to microtitration well. A simple washing step removes unbound enzyme labelled antibody. The bound conjugate is detected by reaction with 3,3',5,5' tetramethylbenzidine (TMB). The reaction is stopped by adding acid to give a colorimetric endpoint that is read spectrophotometrically.

Samples were thawed and sufficient microplate wells were prepared to accommodate calibrators and samples in duplicate. 25 µl of each calibrator and sample were pipetted into each microplate well. Then 100 µl of enzyme conjugate solution was added to each well. One hour incubation on a plate shaker followed at room temperature. Contents of microplate were then aspirated and 350 µl wash buffer was added to each well five times and the contents were aspirated. After drying on absorbent paper 200 µl substrate TMB was added into each well and incubation at room temperature for 15 minutes followed. 50 µl of stop solution was then added to each well and the plate was placed on a shaker

to ensure mixing for approximately 5 seconds. Finally, optical density was read at 450 nm and results were calculated.

Soluble vascular cell adhesion molecule-1 was measured using a commercially available immunoassay kit (R&D Systems Inc, Minneapolis, USA). All samples for each participant were analysed in a single analyser run. The accuracy and precision of the assays was monitored using quality control sera (Mercodia AB, Uppsala, Sweden; R&D Systems Inc, Minneapolis, USA). Assays were performed in the biochemistry laboratory of the Department of Human Nutrition, University of Glasgow. Coefficient of variation was <4%.

2.4.2 Cholesterol, triglycerides, glucose and C-reactive protein measurements

For the study investigating and the effects of two different exercise patterns on physical, fitness and metabolic variables in overweight women, TG, plasma total cholesterol, HDL (Roche Diagnostics Gmbh, Mannheim, Germany) and glucose levels (Randox Laboratories Ltd., Co. Antrim, Ireland) were determined by enzymatic colorimetric methods using commercially available kits in the biochemistry lab of the Department of Clinical Biochemisty, Royal Infirmary, Glasgow. Low-density lipoprotein was calculated using the Friedewald et al., (1972) equation: [LDL-chol] = [Total chol] - [HDL-chol] - ([TG]/2.2) where all concentrations are given in $mmol \cdot l^{-1}$. High sensitivity CRP was measured using an immunoturbidimetric assay (Randox Laboratories, Crumlin, Co. Antrim, UK) in the biochemistry lab of the Department of Clinical

Biochemisty, Royal Infirmary, Glasgow. All samples for each subject were analysed in a single analyser run. Coefficients of variation were <3.1%.

In the study investigating the effect of a single exercise session on appetite, energy intake and metabolic health variables in response to four consecutive *ad libitum* meals in overweight women, TG measurements were made by enzymatic colorimetric method using commercially available kits (Horiba ABX, Montpellier, France). Assays were performed in the biochemistry laboratory of the Institute of Diet, Exercise and Lifestyle (IDEAL), University of Glasgow using a Cobas Mira Plus (ABX Diagnostics, France). The accuracy and precision of the assays was monitored using quality control sera (Horiba ABX, Montpellier, France). Glucose concentration was determined by enzymatic colorimetric methods using commercially available kits (Randox Laboratories Ltd., Co. Antrim, Ireland). All samples for each participant were analysed in a single analyser run. Coefficients of variation were < 3.1%.

2.4.3 Lactate measurement

Lactate analysis was made by fluorimetry according to an altered procedure suggested initially by Maughan (1982) in the biochemistry laboratory of IDEAL, University of Glasgow. A filter fluorimeter (Fluoroscan Ascent FL, Labsystems, Finland) was used and all measurements were made at 340 nm excitation beam. The principle upon which this procedure is based is the interconversion of metabolites linked to a change in the oxidation state of nicotinamide adenine dinucleotide (NAD^+) by the following reaction:

$$\text{L-lactate} + \text{NAD} + {}^{(\text{LDH})} \leftrightarrow \text{pyruvate} + \text{NADH} + \text{H}^{+}$$

Before the analysis standards with concentrations 1 mmol·l^{-1}, 2 mmol·l^{-1}, 3 mmol·l^{-1}, 5 mmol·l^{-1} and quality control (5 mmol·l^{-1}) were diluted with perchloric acid (1/10) and all specimens were brought into room temperature. Reaction mixture was made fresh containing the proportion of 1 ml hydrazine buffer, 50 µl NAD and 10 µl lactate dehydrogenase (LDH). 20 µl of each standard and sample was placed in the wells of the plate (Corning, 96 wells) in duplicates. 200 µl reaction mixture was immediately dispensed over the samples and standards. Incubation and shaking period then followed for 30 minutes. The fluorescence was read after measurement of the determined areas. The blank fluorescence was set to zero. Sample values were obtained then by comparison with the standard curve. Reliability of the results was routinely monitored using quality control (Pointe Scientific, Inc.) that reasonably emulates performance of real specimens.

2.4.4 Homeostasis model assessment of insulin resistance ($HOMA_{IR}$)

Insulin resistance was calculated using the $HOMA_{IR}$, according to which Insulin Resistance = Fasting Glucose* Fasting Insulin/22.5 (Matthews et al., 1985).

Chapter 3: Effect of a single exercise session on appetite, energy intake and metabolic health variables in response to four consecutive *ad libitum* meals in overweight women

3.1 Introduction

Increasing physical activity is one of the strategies recommended for weight maintenance and weight loss (Donnelly et al., 2009). Theoretically the energy expended during exercise should create a negative energy balance leading to body mass and body fat loss. However, many long term exercise interventions identified that achieved reduction in body mass and body fat in some of participants is smaller than the predicted from energy expended (King et al., 2009a,b; King et al., 2008; Barwell et al., 2008). This relative failure is thought to be mainly due to a compensatory increase in energy intake (King et al., 2009a; King et al., 2008; Staten, 1991) and/or a reduction in activity outside exercise sessions (Stubbs et al., 2002a,b; Goran and Poehlman, 1992).

Self-reported energy intake used in exercise studies aiming at identification of compensatory mechanisms preventing from body mass and body fat loss (Barwell et al., 2008; Maraki et al., 2005; Klausen et al., 1999) can be inaccurate and incurs a high level of misreporting especially in overweight and obese populations (Rennie et al., 2007), while studies providing *ad libitum* feeding under controlled conditions allow closer observation of the human behaviour towards appetite and energy intake (Ershow et al., 2004). Most of the studies, which have used *ad libitum* feeding to assess appetite and energy intake in response to a single exercise session, were conducted on lean and

healthy individuals (Bilski et al., 2009; Melzer et al., 2005; Blundell et al., 2003; Blundell and King, 1999) and only very few considered exercise-induced changes in appetite and energy intake in overweight or obese women (George et al., 2003; Tsofliou et al., 2003; Kissileff et al., 1990), a group requiring special attention. Findings from the studies on overweight and obese women, although indicating that exercise does not affect subsequent energy intake, are limited by short post-intervention observation periods ranging from 15 minutes to 1 hour and low exercise-induced EE ranging from approximately 120 to 237 kcal (George et al., 2003; Tsofliou et al., 2003; Kissileff et al., 1990), while it has been suggested that regular exercise sessions with EE of approximately 2 MJ are needed for the achievement of body mass and body fat loss (Donnelly et al., 2009; Saris et al., 2003; Jakicic et al., 2001).

Acute exercise has been shown to attenuate fasting and postprandial concentrations of insulin and plasma TG, which are metabolic risk factors implicated in the development of atherosclerosis and type 2 diabetes (Mestek et al., 2009; Gill and Malkova, 2006, Malkova and Gill, 2006). The impact of exercise, however, on postprandial metabolic changes was mainly investigated by providing participants with a standard fixed-sized meal, which was identical for both exercise and control trials (Malkova and Gill, 2006*;* Gill and Malkova, 2006) and only few studies demonstrated the effect of exercise on metabolic health variables following *ad libitum* feeding (Farah et al., 2010; King et al., 2010a,b), which is more reflective of a "real-life" situation. The latter studies demonstrate that energy deficit induced by a single exercise session can reduce TG

response after consumption of two *ad libitum* meals in overweight/ obese (Farah et al., 2010) but not in lean males (King et al., 2010 a,b).

This study aims to identify the impact of a single moderate intensity exercise session with EE of 2 MJ, which corresponds to the recommended amount of exercise sessions aiming to achieve body weight reduction (Donnelly et al., 2009; Saris et al., 2003; Jakicic et al., 2001), on appetite, energy intake and metabolic health variables in response to four consecutive *ad libitum* meals in overweight and obese females.

3.2 Methods

3.2.1 Participants

Twelve healthy and overweight or obese women were recruited for this study. Baseline physical characteristics are shown in Table 3.1. Exclusion criteria, recruitment and ethical approval process are described in detail in section 2.1 of General Methods. Before trials all participants undertook a familiarisation session where they were given the opportunity to ask questions and to familiarise with experimental equipment. They were then asked to complete questionnaires related to food preferences and eating patterns.

3.2.2 Study design

Each participant undertook two main experimental trials in randomised order (described below and outlined in Figure 3.1) with an interval of 4 weeks to control for the effects of their menstrual cycle. Participants performed either a single cycling session at 65% $\dot{V}$

O_{2max} in order to expend approximately 2 MJ (exercise trial) or rested for the same duration (control trial). Each of these trials was conducted over two days and lasted for approximately 27 hours including overnight at home. Before the first main experimental trial volunteers were asked to attend the laboratory in order to take part to preliminary tests which included body composition and RMR measurements (see General Methods, section 2.2) and exercise testing for prediction of $\dot{V}O_{2max}$ (see General Methods, section 2.3).

3.2.2.1 Physical activity and dietary standardisation

Participants completed a weighed food record of all items consumed within the 2.5 days preceding their first main trial. Alcohol and caffeine were not permitted during this period. On the first day before the commencement of each trial, participants were advised to eat their usual portions of breakfast and lunch at home at ~09:00 h and ~13:00 h, respectively, while recording their weighed food and drinks intake. Participants also refrained from strenuous physical activity during this time. These patterns were replicated prior to the subsequent trial.

3.2.2.2 Main trials

a) Day 1- At approximately ~16:30 h in each trial, participants came to the metabolic investigation suite (Figure 2.1) where a cannula was inserted in an antecubital vein and a baseline blood sample was collected and appetite questionnaires were completed. Afterwards they were transferred to the exercise physiology laboratory and either undertook the exercise trial or stayed in the metabolic room for the same duration resting

quietly in control trial. At the start and end of the cycle or rest time (at 0 and 120 minutes) and at 30 minute intervals (at 150, 180 and 210 minutes) until dinner was served blood samples were taken and appetite questionnaires were completed (Figure 3.1). An *ad libitum* buffet dinner was then provided and the amount of food ingested was recorded. Following the buffet, participants returned home with instructions to avoid eating food until the next day's trial. The amount of food served and water consumed in the first trial were replicated during the second trial.

b) Day 2- On day 2 participants arrived at the metabolic investigation room (Figure 2.1) at ~08:00 h in the fasted state. A cannula was inserted in an antecubital vein and a baseline blood sample was collected and appetite questionnaires filled in. Three *ad libitum* meals were given throughout the day. Breakfast was given at ~09:00 h, lunch was provided 3.5 hours after breakfast and dinner was served 4.5 hours after lunch. Blood samples and appetite questionnaires were repeated before and after breakfast (at 0 and 60 minutes) and every 60 minutes thereafter (at 120, 180, 240, 300, 360, 420, 480 minutes) (Figure 3.1). Lunch consumption commenced at 240 minutes and dinner consumption at 480 minutes.

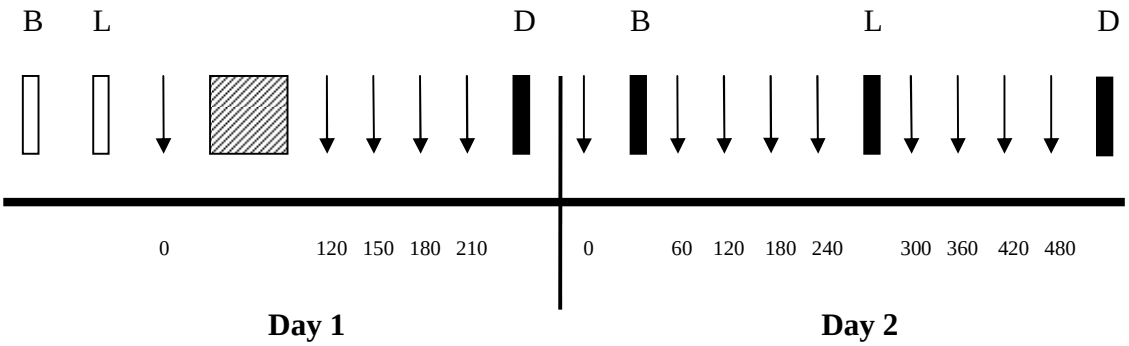


Figure 3.1 Schematic representation of trials on Day 1 and 2.

= standard meal consumed at home; = buffet meal; = blood, appetite questionnaires; = exercise or control intervention; B, breakfast; L, lunch; D, dinner.

3.2.3 Calculation of exercise intensity and duration

In order to calculate exercise intensity of the acute exercise session, $\dot{V}O_2$ and $\dot{V}CO_2$ obtained in exercise testing were plotted against HR, regression equations for both $\dot{V}O_2$ and $\dot{V}CO_2$ were generated and values at 65% $\dot{V}O_{2max}$ were calculated. $\dot{V}O_2$ was also plotted against intensity (W) and intensity at 65% of $\dot{V}O_{2max}$ was found. Individual rate of ExEE at 65% of $\dot{V}O_{2max}$ was then calculated using indirect calorimetry equations (Frayn and Macdonald, 1997). In order to calculate duration of the exercise session the required gross ExEE (2000 kJ) was divided by the individual rate of EE ($kJ \cdot min^{-1}$). Duration of the cycling differed between individuals, ranging from 52 to 89 minutes and corresponding HR was 133 ± 7.7 beats$\cdot min^{-1}$.

3.2.4 Exercise session

The acute exercise session was conducted at least 3 hours postprandially, after participants had lunch on the first day of the two-day trial. Exercise sessions were conducted on a cycle ergometer (Ergomedic 873, Monark, Sweden) at 65% $\dot{V}O_{2max}$ at a steady cadence in order to expend approximately 2 MJ. Heart rate was continuously recorded by short-range telemetry (Polar S610i, Polar Electro Oy, Kempele, Finland) and ratings of RPE (Borg, 1974) were recorded at 15-minute intervals during the exercise to ensure that they were working at a consistent and safe level. Heart rate data were downloaded to a University laptop computer through an infrared port using Polar software (Polar Electro Oy, Kempele, Finland) after the end of the exercise session. Expired air samples were obtained for 2 minutes every 15 minutes through Douglas bags and were immediately analysed through a gas analyser (Servomex 4000 series, Servomex Group Limited, East Sussex, UK) (see General Methods, section 2.3). Water consumption was allowed while exercising and was monitored in order to duplicate quantities during the two trials, exercise and control.

3.2.4.1 Calculation of exercise energy expenditure

In order to calculate substrate oxidation and gross ExEE, equations of indirect calorimetry were applied using $\dot{V}O_2$ and $\dot{V}CO_2$ values obtained in the exercise session (Frayn and Macdonald, 1997). Net ExEE was calculated by subtracting RMR equivalent for the exercise time from gross ExEE.

3.2.5 *Ad libitum* buffet meals

Ad libitum buffet meals were provided four times during the two consecutive days; on Day 1 (dinner meal) and Day 2 (breakfast, lunch, and dinner meals). The buffet consisted of a wide range of standardised foods according to participants' preferences approximately 3 times in excess of their expected consumption. *Ad libitum* buffet-style breakfast contained a variety of breakfast cereals, semi-skimmed milk, croissants, margarine, jam, fruits (banana, kiwi or clementine, grapes) and orange juice yielding a total of 9.8 MJ of energy (Figure 3.2). *Ad libitum* buffet-style lunch contained two filled white bread sandwiches, two filled wholemeal bread sandwiches, soup (vegetable or chicken), salad, vinaigrette sauce, profiterole or cheesecake, fruits (banana, kiwi or clementine, grapes) and orange juice yielding a total of 11.2 MJ of energy (Figure 3.3). Finally, both dinners contained a standard cooked meal (from frozen), bread, salad, vinaigrette sauce, fruit yogurt, profiterole or cheesecake, fruits (banana, kiwi or clementine, grapes) and orange juice yielding a total of 14.8 MJ of energy (Figure 3.4).

The buffet foods were identical in the two trials, of the same energy and macronutrient content and provided diversity in protein, fat and carbohydrate content in order to facilitate the detection of macronutrient preferences. All foods were covertly weighed before they were made available to subjects and re-weighed again after meal ingestion to quantify food intake. Where possible, food was cut in smaller pieces in order to eliminate portion-size related cues. Participants were told to eat until satisfied during the 30 minutes given to consume their meal and that additional food was available if desired. Water was not provided during the meals but *ad libitum* access to water was made available throughout the first trial and was replicated on the second one.

Experimenters were not present when subjects consumed the buffets in order to minimise any potential effects of experimenter presence on feeding behaviour. Participants were also blinded to the purpose of the buffet meals (i.e. measuring food intake), and were instead told that blood biomarkers in relation to food consumed were investigated. This strategy reduced the potential bias that could occur if a person was consciously aware that food consumption is being monitored as eating patterns and behaviour can be affected by a number of emotional and cognitive beliefs and restraints, especially with regards to the volume of food that is consumed and types of food that are perceived “good or bad” (Herman and Polivy, 2005).

Total energy intake and macronutrient content of food and drinks consumed before and during trials were assessed using WinDiet software (The Robert Gordon University, Aberdeen, Scotland, UK).

Figure 3.2 *Ad-libitum* buffet style breakfast presentation

Figure 3.3 *Ad-libitum* buffet style lunch presentation

Figure 3.4 *Ad-libitum* buffet style dinner presentation

3.2.6 Appetite measurements

Appetite sensations were measured by appetite questionnaires. Participants were asked to rate their hunger, satiety, fullness and PFC and DTE on 100mm lines (Flint et al., 2000), (Appendix VI). The four questions were anchored on the left by the negative

respective feeling and on the right by the positive respective feeling. Subjects were asked to make a mark across the line corresponding to their feelings. Quantification of the measurement was made by measuring the distance from the left end of the line to the mark.

3.2.7 Blood collection and analysis

Blood collection took place in the metabolic investigation suite (Figure 2.1). Venous blood samples were taken at several time points (Figure 3.1) and used to measure glucose, insulin and TG. Samples were collected using an indwelling 18G cannula (Venfoln, BOC, Helsingbourg, Sweden) inserted into a forearm antecubital vein into a 7.5ml ethylenediamine tetra-acetic acid (EDTA) Vacutainer™ tube (BD Vacutainer Systems, Plymouth, UK) and were placed on ice prior to centrifugation at 4°C, 3000 rpm for 15 minutes. Plasma was aspirated after centrifugation using a disposable plastic Pasteur pipette and then dispensed in 6-8 0.5 ml aliquots into labeled 2 ml eppendorfs (Alpha Laboratories Ltd, UK), and frozen at -80ºC until analysis. For the duration of the trial the cannula was kept patent by injection of 5 ml of sterile saline solution (0.9% sodium chloride BP; B. Braun Medical Ltd., Bucks, England) at 30 minute intervals. Residual saline in the dead space was drawn off and discarded prior to sampling. Glucose, insulin and TG concentrations were then determined (see General Methods, section 2.4).

3.2.8 Statistical analysis and power calculations

Data were firstly tested for normality using the Anderson-Darling test (Minitab, version 13.1, Minitab Inc., State College, Pennsylvania) and were found to be normally distributed. Statistical analysis was then performed using Statistica (version 6.0, StatSoft Inc., Tulsa, USA). The total areas under response versus time curve (AUC), calculated using the trapezium rule, were used as summary measures of the postprandial responses. One-way repeated measures ANOVA was used to compare energy intakes of four meals between the two trials. Two-way repeated measures ANOVA (trial x time) was used to compare appetite and metabolic responses between trials and evaluate changes over time. *Post hoc* Tukey tests were used to identify where differences lay. Student's *t*-tests for correlated data were used to assess differences between fasting values and AUCs calculated for appetite and metabolic variables. Data are presented as means ± SEM, unless otherwise stated. Statistical significance was accepted at $p < 0.05$.

Power calculations were performed using Minitab (version 13.1, Minitab Inc., State College, Pennsylvania). Based on previously obtained data, power calculation indicated that to find significant difference with 85% power in appetite measures when difference of means between trials is 6.6 mm and SD for this difference is 6.6, 12 participants are required (Malkova et al., 2008). Power calculation also identified that 10 subjects would allow to detect a difference of 0.13 $mmol \cdot l^{-1}$ in TG **and 10% difference in insulin between** trials with 85% power when SD for this difference is 0.12.

3.3 Results

Mean gross ExEE of the exercise session was (mean ± SD) 2.02 ± 0.18 MJ and net ExEE was 1.71 ± 0.15 MJ at HR 133 ± 7.7 beats·min^{-1}, intensity of 65.0 ± 30.6 W and total duration was 72.8 ± 12.0 minutes. The rate of fat and carbohydrate oxidation during exercise was 0.21 ± 0.03 g·min^{-1} and 1.25 ± 0.08 g·min^{-1} respectively. There were no significant differences in any baseline characteristic between the two groups (Table 3.1).

Table 3.1 Subject characteristics at baseline. Values are mean ± SD

	n = 12
Age (years)	36.9 ± 8.3
Height (cm)	157.9 ± 5.8
Body mass (kg)	76.1 ± 10.6
BMI (kg·m^{-2})	30.5 ± 3.6
Fat mass (kg)	29.8 ± 7.8
Fat %	38.6 ± 4.9
Fat free mass (kg)	46.3 ± 3.6
RMR (MJ·d^{-1})	6.29 ± 0.47
$\dot{V}O_2$max (ml·kg·min^{-1})	29.00 ± 4.31

Abbreviations. BMI, body mass index; RMR, resting metabolic rate; $\dot{V}O_2$max, maximal oxygen uptake.

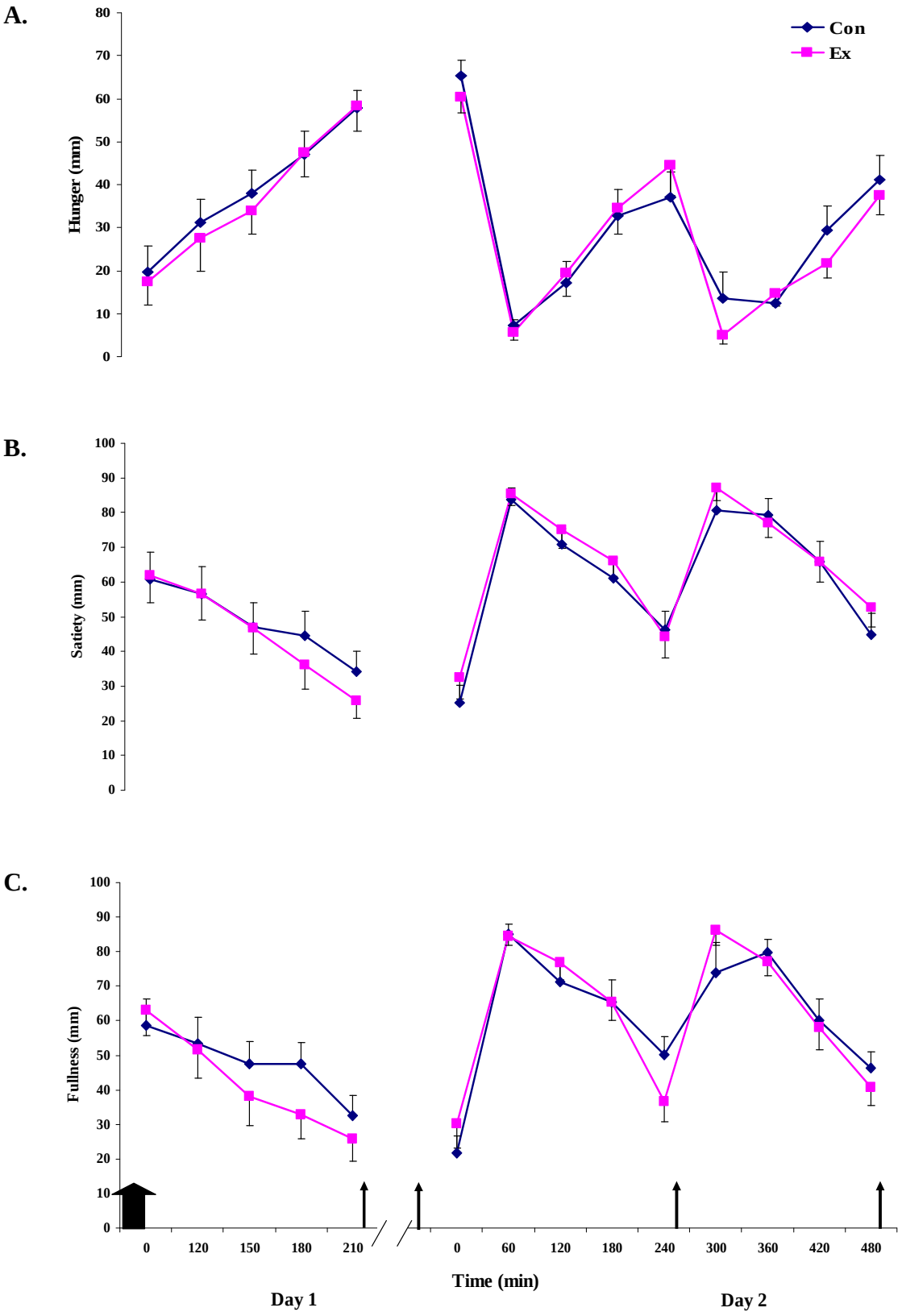
3.3.1 Responses of appetite and energy intake

3.3.1.1 Appetite responses on Day 1

Data on appetite responses for exercise and control trials are presented in Figure 3.5. On Day 1 hunger, satiety, fullness, and DTE were not significantly different between exercise and control trials, while PFC was significantly lower following exercise ($p<0.05$, Two-way ANOVA, trial effect). *Post hoc* analysis revealed that PFC was significantly lower in the exercise trial immediately and 30 minutes after exercise ($p<0.05$, for both time points). Changes over time for all appetite measures were significant ($p<0.001$, Two-way ANOVA, time effect). Summary measures of all appetite responses evaluated as time averaged AUC were not significantly different between exercise and control trials.

3.3.1.2 Appetite responses on Day 2

Data on appetite responses for exercise and control trials are presented in Figure 3.5. On Day 2 hunger, satisfaction, fullness, PFC and DTE were not significantly different between exercise and control trials. There was a main effect of time for all appetite measures ($p<0.001$, Two-way ANOVA, time effect). Summary measures of appetite responses evaluated as time averaged AUC are presented in Table 3.2. Time averaged AUC over post breakfast, post lunch and over whole period of Day 2 for all appetite measures were not significantly different between exercise and control trials.


A.
B.
C.
Con
Ex
Hunger (mm)
Satiety (mm)
Fullness (mm)
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30
40
50
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70
80
90
100
0
120
150
180
210
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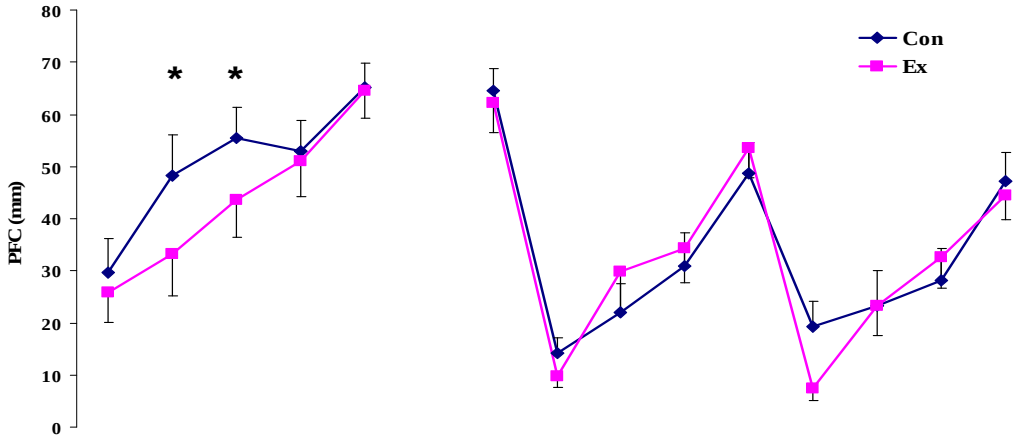
60
120
180
240
300
360
420
480
Time (min)
Day 1
Day 2

D.



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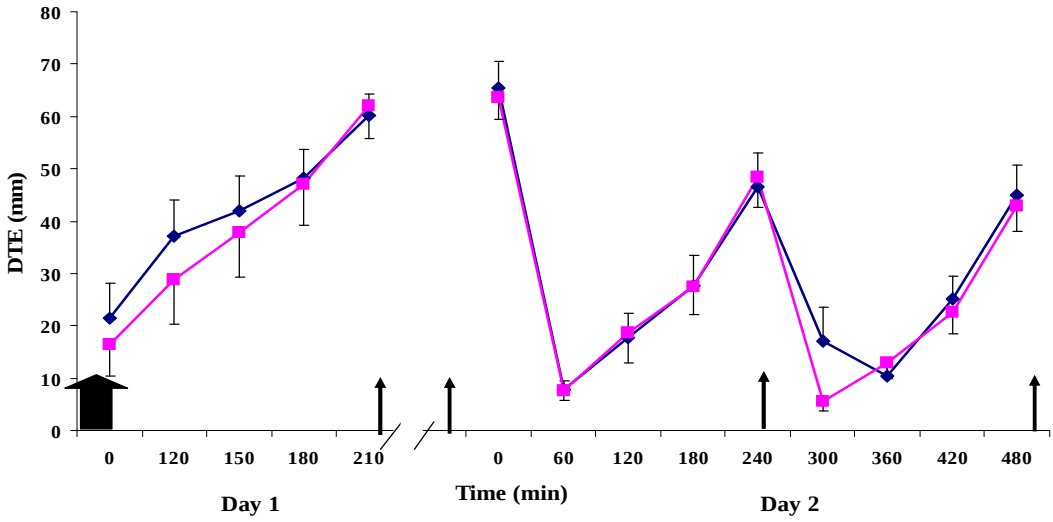


Figure 3.5 Appetite scores for hunger (A), satiety (B), fullness (C), prospective food consumption (PFC) (D) and desire to eat (DTE) (E) measured with the use of visual analogue scales in control (Con) and exercise (Ex) trials on Day 1 and Day 2. Values are mean ± SEM.

* significantly different ($p < 0.05$) from exercise trial. ⬆ = exercise/ control period; ↑ = ad libitum meal

Table 3.2 Time averaged areas under response versus time curves (AUCs) for hunger, satiety, fullness, prospective food consumption (PFC) and desire to eat (DTE) in control (Con) and exercise (Ex) trials after breakfast and after lunch on Day 2. Values are mean ± SEM.

	AUCs			
	Breakfast		Lunch	
	Con	Ex	Con	Ex
Hunger (mm)	33.4 ± 3.1	34.2 ± 3.1	24.1 ± 2.4	21.1 ± 2.6
Satiety (mm)	78.6 ± 4.1	82.7 ± 3.6	66.6 ± 4.4	69.5 ± 4.4
Fullness (mm)	80.0 ± 4.9	80.4 ± 3.0	66.7 ± 3.6	64.5 ± 4.5
PFC (mm)	39.4 ± 3.9	40.5 ± 3.6	30.3 ± 4.1	28.6 ± 4.0
DTE (mm)	35.3 ± 3.4	34.2 ± 3.4	25.0 ± 2.9	22.1 ± 2.8

3.3.1.3 Energy intake on Day 1 and Day 2

Energy and macronutrient intake consumed in the buffet meals at dinner (Day 1) and breakfast, lunch and dinner (Day 2) in exercise and control trial were not significantly different between trials (Table 3.3). The proportion of energy obtained from carbohydrate (Control, 53.9 ± 2.4%; Exercise, 53.2 ± 2.4%), fat (Control, 34.3 ± 2.4%; Exercise, 35.4 ± 2.7 %) and protein (Control, 11.8 ± 0.8%; Exercise, 11.4 ± 1.0%) did not differ between trials for all four *ad libitum* meals. Relative energy intake (absolute

energy intake - net ExEE), was significantly higher after control than exercise trial (Control, 16.27 ± 1.24 MJ; Exercise, 15.05 ± 1.58 MJ, p= 0.03).

3.3.2 Metabolic responses

3.3.2.1 Metabolic responses on Day 1

Due to difficulties with blood sampling in two participants, data for plasma variables are presented for n = 10. Data on glucose, insulin and TG responses are presented in Figure 3.2. On Day 1 glucose, insulin and TG were not significantly different between exercise and control trials. Changes over time for insulin and TG were significant ($p<0.001$, Two-way ANOVA, time effect). Summary measures of concentrations evaluated as time averaged AUC for all metabolic variables were not significantly different between exercise and control trials.

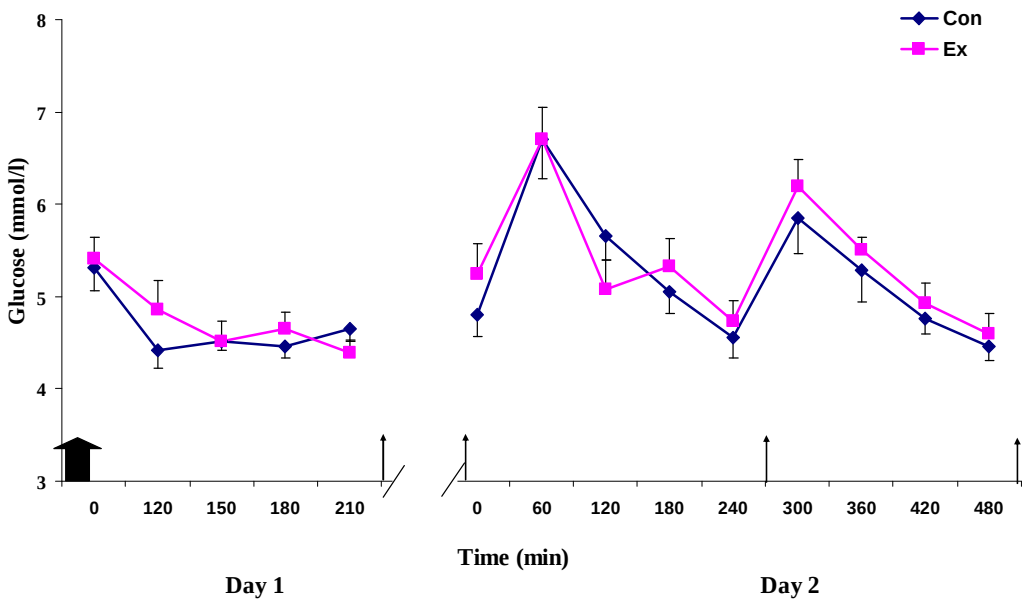
Table 3.3 Energy, fat, carbohydrate (CHO) and protein intake during four *ad libitum* buffet meals in control (Con) and exercise (Ex) trials. Values are mean ± SEM.

	DAY 1		**DAY 2**					
	Dinner		**Breakfast**		**Lunch**		**Dinner**	
	Con	**Ex**	**Con**	**Ex**	**Con**	**Ex**	**Con**	**Ex**
Energy intake (MJ)	4.76 ± 0.35	4.97 ± 0.50	3.29 ± 0.32	3.14 ± 0.4	4.33 ± 0.49	4.51 ± 0.47	4.20 ± 0.37	4.14 ± 0.52
Fat intake (MJ)	1.88 ± 0.21	1.99 ± 0.31	0.66 ± 0.10	0.65 ± 0.09	1.62 ± 0.25	1.66 ± 0.26	1.56 ± 0.24	1.66 ± 0.29
CHO intake (MJ)	2.32 ± 0.20	2.44 ± 0.26	2.30 ± 0.25	2.17 ± 0.31	2.25 ± 0.31	2.37 ± 0.29	2.11 ± 0.19	1.99 ± 0.26
Protein intake (MJ)	0.58 ± 0.06	0.57 ± 0.06	0.36 ± 0.03	0.34 ± 0.03	0.48 ± 0.04	0.51 ± 0.03	0.55 ± 0.06	0.52 ± 0.06

3.3.2.2 Metabolic responses on Day 2

Glucose, insulin and TG responses are presented in Figure 3.6. On Day 2 glucose, insulin and TG were not significantly different between exercise and control trials, however, there was a main effect of time for all metabolic variables ($p<0.001$, Two-way ANOVA, time effect). Summary measures of concentrations evaluated as time averaged AUC are presented in Figure 3.7. Time averaged AUCs for insulin and glucose measured after breakfast, were not significantly different between trials. Time averaged AUC for TG measured after breakfast, was significantly lower in exercise than control trial ($p=0.04$, t-test for paired data). Time averaged AUC for glucose and insulin measured after lunch, were not significantly different between trials, while time averaged AUC for TG tended to be lower in the exercise trial ($p=0.07$, t-test for paired data).

A.



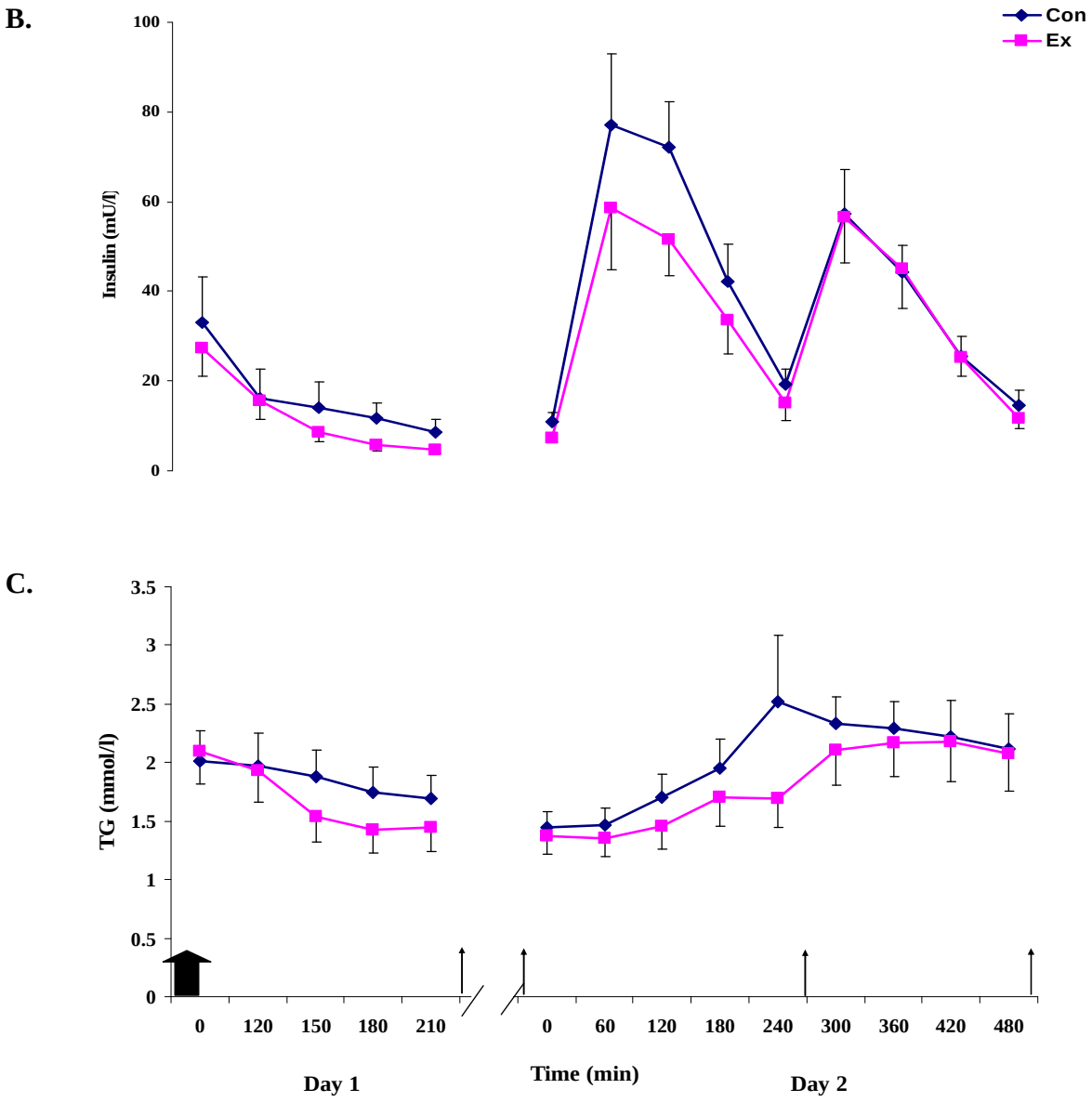


Figure 3.6 Mean concentrations for plasma glucose (A), insulin (B) and triglycerides TG (C) concentrations in control (Con) and exercise (Ex) trials on Day 1 and Day 2. Values are mean ± SEM. ⬆ = exercise/ control period; ↑ = ad libitum meal

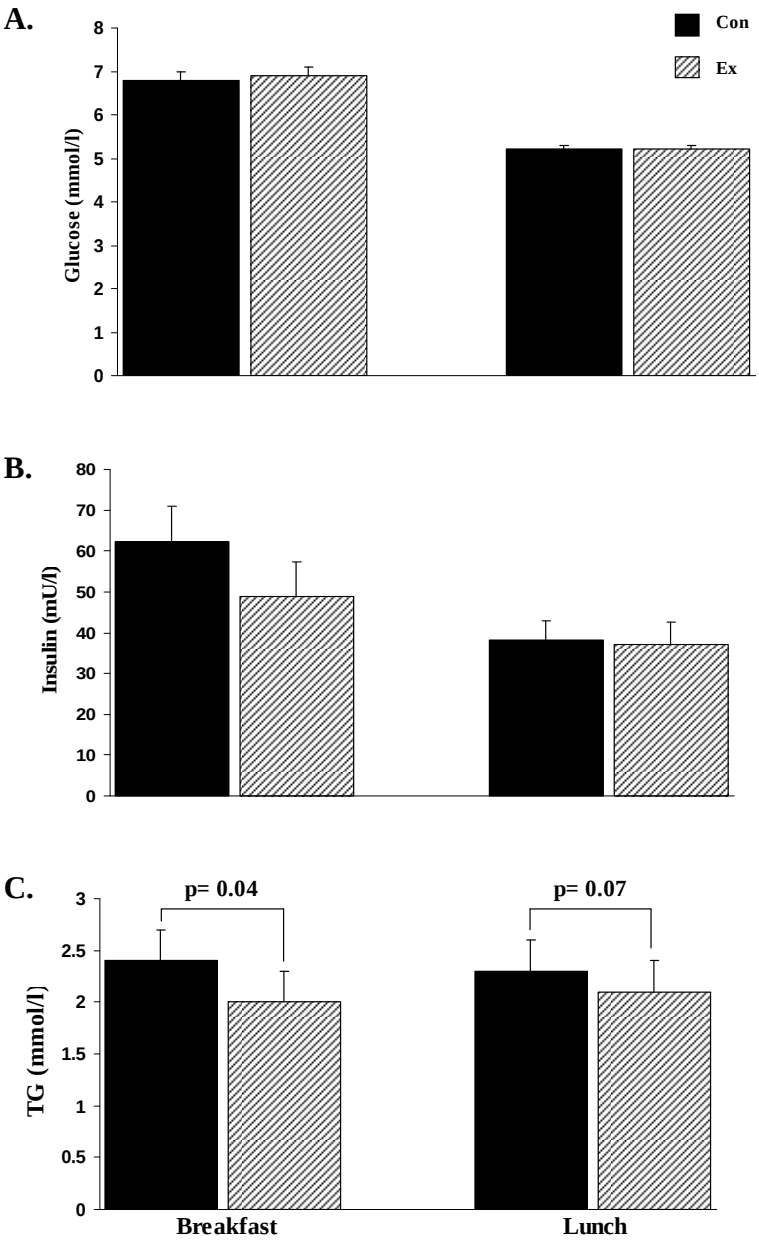


Figure 3.7 Time averaged areas under response versus time curves (AUCs) for glucose (A), insulin (B) and triglycerides (TG) (C) in control (Con) and exercise (Ex) trials after breakfast and after lunch on Day 2. Values are mean ± SEM.

3.4 Discussion

The main findings of this study are that a single exercise session with EE of 2 MJ, which is in line with the EE recommended for individual exercise sessions aiming at body weight and body fat reduction (Donnelly et al., 2009; Saris et al., 2003; Jakicic et al., 2001) conducted in sedentary overweight and obese women, does not elicit compensation in appetite and energy intake. Furthermore, it was found that postprandial TG responses to *ad libitum* breakfast consumed approximately 14 hours after exercise were significantly lower than in control trial.

The finding that energy intake of four meals eaten *ad libitum* over 2 consecutive days in the current study was the same between control and exercise trials, is in agreement with previous findings, which have shown no impact of acute exercise session on energy intake measured for the duration of 1 or 2 days in lean (Maraki et al., 2005; Lluch et al., 1998; King et al., 1997; Almeras et al., 1995; Tremblay et al., 1994; King et al., 1994) or overweight/ obese individuals (Farah et al., 2010). Furthermore, REI, calculated as absolute energy intake minus net ExEE (King et al., 1997), was significantly lower after exercise (15.05 ± 1.58 MJ) in comparison with control trial (16.27 ± 1.24 MJ). Thus, individuals in the exercise trial indeed did not compensate for ExEE, which lends support for the utility of exercise in successful body weight control. However, that does not exclude the possibility that full or partial compensation may happen in later stages following an acute exercise session (Blundell et al., 2003; Blundell and King, 1999), or at some point within exercise programmes (King et al., 2008). It is interesting to note, that as it has been previously identified (Finlayson et al., 2009), individual compensatory

differences may exist after a single bout of exercise.Therefore, individual predisposition to compensate for exercise-induced EE might be a reason for the relative failure to lose weight seen in long term exercise interventions.

As energy intake during breakfast, lunch and dinner on Day 2, subjective appetite measures were also not significantly different between trials, a finding which is in accordance with another study measuring appetite on the next day following a single exercise session (King et al., 1997). On Day 1, regardless of PFC being significantly lower in the early post exercise period (immediately and approximately 30 minutes after exercise), difference in energy intake during dinner was not significant between trials. The finding that the short-lived suppression of appetite following acute exercise is not translated into reduced energy intake is consistent with some studies conducted on lean individuals (King et al., 1994; Thompson et al., 1988) and obese women (Tsofliou et al., 2003) but differs from findings obtained in other studies (Ueda et al., 2009a,b; Martins et al., 2007b; Westerterp-Plantenga et al., 1997). It is reported previously, however, that the short-lived suppression of hunger could be independently related to redistribution of blood flow occurring during exercise and it is mostly observed after high-intensity exercise is undertaken (Blundell et al., 2003).

This is one of the few studies (Farah et al., 2010; King et al., 2010a,b) investigating postprandial responses of insulin, glucose and TG, following a series of *ad libitum* meals. This study found that response of TG was significantly lower after *ad libitum* breakfast consumed approximately 14 hours after exercise and tended to be lower after

ad libitum lunch consumed approximately 18 hours after exercise than control intervention. Diminished impact of exercise on TG responses after lunch in comparison to after breakfast is not surprising since it is well documented that the effects of exercise on postprandial lipaemia are relatively short-lived, with the maximal effect observed approximately 8-16 hours post-exercise (Gill and Hardman, 2003) or up to an 18-hour time window (Zhang et al., 1998) and markedly diminishing from 24 hours onwards (Ferguson et al., 1998). This reduction in TG responses after meals consumed on the next day following exercise is of a great importance since increase in postprandial lipaemia is one of the independent risk factors for the development of atherosclerosis (Malkova and Gill 2006; Petitt and Cureton, 2003). Indeed, elevated concentration of TG rich lipoproteins in the postprandial state accelerates the generation of atherogenic lipoprotein remnant particles (Cohn, 1998; Karpe, 1999) and contributes to an indirect atherogenic effect by facilitating preponderance of highly atherogenic small dense LDL and low concentrations of atheroprotective HDL (Griffin, 1997).

The vast majority of studies investigating the effects of exercise on postprandial lipaemia have used isocaloric test meals with a high-fat content (at least of 60% of energy from fat) which greatly exceeds the usual fat intake in a typical western diet (Malkova and Gill, 2006), while some studies have used fixed-size meals of 35% energy deriving from fat, which is more representative of the percentage of fat ingested in habitual diet (Burton et al., 2008; Pfeiffer et al., 2006; Pfeiffer et al., 2005; Kokalas et al., 2005; Petridou et al., 2004; Kolifa et al., 2004). Data obtained from all the above studies suggest that exercise reduces postprandial lipaemia by 26-35%. In contrast

participants of the current study consumed *ad libitum* meals with approximately 35% of energy deriving from fat, which reflects food consumption in "real-life" situation. Under these circumstances still, it was found that after *ad libitum* consumption of breakfast 14 hours after intervention postprandial lipaemia was lower by 17% in the exercising group. Similarly, Farah and colleagues (2010) in a study using *ad libitum* meals reported that following exercise with EE of 2.98 MJ, postprandial lipaemia was reduced by 17% in overweight /obese men. Therefore, current findings obtained from studies investigating postprandial lipaemia on overweight/obese individuals suggest, that the exercise-induced attenuation of postprandial TG concentrations persists when meals are consumed *ad libitum*. This might suggest that the TG-lowering effect of prior exercise extends into a "real-world" setting where food intake is not carefully controlled.

This study revealed no significant change in postprandial insulin and glucose following an exercise session with EE of 2 MJ, evidence which is in consistency with other studies investigating postprandial lipaemia under *ad libitum* feeding conditions (Farah et al., 2010; King et al., 2010 a,b) or with those providing fixed-size meals (Malkova et al., 2000). Although it is suggested that insulin sensitivity and responsiveness measured by euglycaemic-hyperinsulinemic clamp has been improved for at least 2 days following a single session of exercise (Perseghin et al., 1996; Mikines et al., 1988), measuring only insulin concentrations does not preclude an effect on insulin action. Moreover, no difference in glucose concentration does not necessarily mean that exercise did not alter glucose metabolism, but most likely suggests that glucose uptake in skeletal muscle was

increased through insulin-independent mechanisms (Holloszy, 2005; Christ-Roberts and Mandarino, 2004; Long et al., 2004; Zierath, 2002).

One of the strengths of this study is that appetite, energy intake and metabolic responses were measured after four consecutive *ad libitum* meals. This allowed energy intake to be measured more precisely in comparison to other studies, which used self-recorded energy intake. On the other hand buffet meals were consumed under laboratory conditions, which constitute a limitation of the study and might affect participant's behaviour towards food intake (Herman and Polivy, 2005). It is also of interest, that recent research investigating postprandial lipaemia after several *ad libitum* meals used overweight/obese (Farah et al., 2010) or lean men (King et al., 2010a,b), while the current study focused in women who may respond in a different way to men towards energy intake (Donnelly et al., 2005; Stubbs et al., 2002a,b).

Most of the recent studies of this nature in addition to appetite and energy intake measures are aiming to obtain information on changes in plasma hormones supposed to be related with appetite regulation; however, findings are quite inconsistent (Hagobian and Braun, 2010). In the present study, hormones related to appetite were not measured, which limits mechanistic interpretation of the data obtained. However, in principle, these measurements would add no additional value to the measurements of energy intake, which on its own allows understanding of compensatory changes in energy balance.

The training session in order to expend approximately 2 MJ of energy was well tolerated by participants of this study who had average BMI of 30.5 $kg \cdot m^{-2}$ and average body fatness of 38.6%. It would be of interest to find how the exercise session used in this study would be tolerated by severely obese individuals with BMI over 35 $kg \cdot m^{-2}$ and the impact that exercise has on their energy balance and metabolic profile. Future research should also aim to compare the response to single exercise session with the response to a final exercise session of a long term exercise intervention directed to reduce obesity. Data comparison would allow deciding whether energy intake compensators can be identified at the beginning of the training programme and therefore targeted with advice and/ or counselling. There is also a need for future studies to consider extended periods of observation following exercise while participants are fed *ad libitum*. This will allow investigation of possible energy intake compensation in later stages following an acute exercise session.

In conclusion, this study demonstrated that sedentary overweight and obese women undertaking a single cycling session with EE in line with the amount recommended for weight loss (Donnelly et al., 2009; Saris et al., 2003; Jakicic et al., 2001), do not compensate by increasing food intake measured during four *ad libitum* meals. In addition, it was found that this type of exercise favourably modifies responses of TG to *at libitum* breakfast consumed approximately 14 hours following an exercise session. Therefore it is suggested that exercise interventions with exercise sessions of similar amount of EE may be expected to have a significant role for weight management and favourably change metabolic profile in obese and/or overweight individuals.

Chapter 4: Changes in energy intake and energy expenditure components in response to exercise training in overweight women

4.1 Introduction

Increasing TEE by increasing physical activity is an important component of many lifestyle interventions aimed at reducing obesity and its complications. Such increases in TEE should aid body fat and body weight loss, provided all other variables affecting energy balance are kept constant. However, exercise-induced perturbations to energy balance may initiate behavioural compensatory adjustments and either alter food intake (McLaughlin et al., 2006; Stubbs et al., 2002; King et al., 1996; Westerterp et al., 1992; Staten, 1991) or cause a reduction in normal daily activities (Donnelly et al., 2005; Kempen et al., 1995; Goran and Poehlman 1992; Westerterp et al., 1992). This compensation for the exercise-induced energy deficit may explain why exercise alone often does not result in successful weight loss in obese and overweight individuals (Franz et al., 2007).

Despite the commonly reported and accepted notion that the effectiveness of exercise in inducing body fat loss is low, an accumulating body of evidence suggests that the interindividual variability in body weight and fat changes in response to an exercise intervention is large and that participants of exercise intervention studies can broadly be separated into “responders” that is, those who achieve a body fat loss in response to exercise, and “nonresponders” that is, those who fail to achieve a body fat reduction in response to exercise (King et al., 2008; King et al., 2007; Blundell et al., 2003). This

suggests that studies investigating exercise-induced compensatory mechanisms should focus on individual variability rather than consider body fat or body weight changes in the group as a whole. In addition, such studies should ensure adherence to prescription of exercise because variability in the effectiveness of exercise in relation to body fat loss could be accounted for difference in compliance (Colley et al., 2008; Donnelly et al., 2003).

Data evaluating individual responsiveness to exercise induced fat loss are very limited. A study by King et al., (2008) investigated compensatory responses to a supervised and well-controlled exercise programme in overweight men and women in relation to individual variability. The authors reported that participants who experienced a lower than predicted weight loss demonstrated a compensatory increase in their energy intake over the course of the intervention and that those who lost more weight than predicted decreased energy intake, although there was no overall difference before and after the intervention for the group as a whole. Although compensating for exercise-induced energy disturbance could also include alterations in physical activity in nonexercise time (Donnelly et al., 2005; Stubbs et al., 2002; Kempen et al., 1995; Goran and Poehlman 1992), this was not investigated in the aforementioned study.

The aim of the present study was therefore to examine the extent to which changes in physical activity outside of the exercise intervention and energy intake contribute to individual differences in body fat loss induced by exercise training programmes. The volume of exercise used was based on current exercise recommendations (Haskell et al.,

2008), and compliance to the prescribed exercise was ensured by supervision of all exercise sessions.

4.2 Methods

4.2.1 Participants

Thirty-four overweight or obese women were recruited for this study. Baseline physical characteristics are shown in Table 4.1. Exclusion criteria, recruitment and ethical approval process are described in detail in section 2.1 of General Methods.

4.2.2 Study design

Participants performed an 8-week supervised exercise programme, undertaking 150 minutes of exercise per week at HR ranging from 135 to 145 beats·min^{-1}, which corresponded to 72%–77% of their age-predicted HR_{max}. An 8-week intervention period was chosen to ensure that the trial was long enough to induce measurable changes in body composition but short enough to ensure high exercise compliance. During the week preceding the exercise programme (baseline) and during the last week of the exercise programme (week 8), participants were required to wear HR monitors during all waking hours and to record activities and dietary intake in physical activity and food intake diaries. On the morning of the first and the morning after the last exercise session, measurements of body composition, RMR (see General Methods, section 2.2) and waist circumference were obtained, and LT, $\dot{V}O_{2max}$ and the individual relationship of $\dot{V}O_2$ and $\dot{V}CO_2$ to HR during different states were determined (see General Methods, section 2.3).

4.2.3 Determination of the relationship of $\dot{V}O_2$ and $\dot{V}CO_2$ to HR during active and inactive conditions

The approach described by Moon and Butte (1996) was used to establish the relationship between $\dot{V}O_2$ and $\dot{V}CO_2$ to HR during active and inactive conditions. This method combines HR and physical activity measures with nonlinear and discontinuous models to calculate EE and shows good agreement with EE measurements made using room calorimetry. Participants were asked to avoid strenuous activities on the day of testing and on the day before testing. The individual relationships between HR and $\dot{V}O_2$ and HR and $\dot{V}CO_2$ were determined by analysis of expired air samples collected while participants performed activities categorised as "inactive" or "active" (Moon and Butte, 1996). The inactive stage involved participants sitting still for 30 minutes, whereas active stages included activities representative of physical activity in habitual daily life such as standing still, standing while swaying arms, slow and faster walking on a treadmill at self-selected speeds, and finally cycling at gradually increasing intensities beginning at 50W and reaching 105–120W, depending on individual fitness level. Individual regression analyses on the relationships obtained for HR versus $\dot{V}O_2$ and HR versus $\dot{V}CO_2$ were performed to obtain coefficients (a_1, a_2, a_3, a_4, b_1, b_2, b_3, and b_4) specific to each subject: $\dot{V}O_2 = a_1 + b_1 \times HR^3$, and $\dot{V}CO_2 = a_2 + b_2 \times HR^3$ for inactive activities; and $\dot{V}O_2 = a_3 + b_3 \times HR$, and $\dot{V}CO_2 = a_4 + b_4 \times HR$ for active activities (Moon and Butte, 1996). The coefficients generated from this procedure were used for EE calculations, described in the section below. Determination of the relationship of $\dot{V}O_2$ and $\dot{V}CO_2$ to HR during active and inactive conditions was repeated in week 4 to account for adaptive changes due to exercise training.

4.2.4 Recording of physical activity

All activities carried out during the week leading to the exercise programme and during week 8 were written down by participants in a 24-hour physical activity diary (Appendix VIII) with 5-minute accuracy for seven consecutive days (Pols et al., 1996). This diary approach has been shown to have high reproducibility for the assessment of EE (intraclass correlation coefficient = 0.96) (Bouchard et al., 1983) and is often used as the criterion measure in the validation of physical activity questionnaires (Pols et al., 1996), although in the present study it was only used for the classification of activity type. Activities were defined as sleeping, sitting, standing, walking, self-care, driving, and exercise in the diaries and were divided by researcher into three classifications: "sleeping", "inactive" (sitting including driving), and "active" (all activities excluding sitting, driving, and sleeping). Volunteers were also asked to record any miscellaneous activities that did not belong to the specific categories described above. Miscellaneous activities were again classified according to the level of activity (e.g., watching TV would be classified as an inactive activity, whereas washing the dishes would be classified as an active activity). Participants completed 88% of the available time in their activity diaries. The completion rate was not significantly different between responders and nonresponders. For missing data, an inactive or an active activity classification was assigned using the researchers' judgment, according to the nature of activities undertaken immediately before and after the period of missing data and from HR over the missing data period.

4.2.5 Exercise intervention

All participants undertook 150 minutes of supervised exercise per week. To enable addressing a secondary question concerning whether frequency of exercise influenced the extent of fat loss in response to exercise training, participants were randomly assigned to one of two patterns of exercise: exercising twice per week for the duration of 75 minutes (pattern A, n = 18) or exercising five times per week for the duration of 30 minutes (pattern B, n = 16). The participants who exercised for the duration of 75 minutes were allowed one break for the duration of 5 minutes. Exercise sessions were all performed under laboratory conditions on friction-braked cycle ergometers (Ergomedic 873, Monark, Sweden). The intensity of the exercise was individually set at 90% of the LT for the first 2 weeks followed by 95% of the LT for the next 2 weeks. Lactate threshold was reassessed after week 4 of the intervention; exercise intensity was 90% of the new LT for the next 2 weeks and 95% of this value for the final 2 weeks of the programme (see General Methods, sections 2.3 and 2.4). Heart rate was continuously recorded through short-range telemetry HR monitors (Polar S610i; Polar Electro Oy) to ensure that individuals were working at a consistent and safe level and then HR data were downloaded to a University computer through an infrared port using Polar software (Polar Electro Oy, Kempele, Finland) for further analysis. Exercise sessions were performed at a time convenient for participants at least 3 hours postprandially and were supervised by a researcher.

4.2.6 Waist circumference

A waist circumference measurement was taken at the level of the narrowest point between the lowest costal (rib) border and the iliac crest. If there was no obvious

narrowing then the measurement was taken at the midpoint between these two landmarks. The researcher was standing in front of the subject to correctly locate the narrowing of the waist. The measurement was taken at the end of a normal expiration with the arms relaxed at the sides.

4.2.7 Calculation of energy expenditure

Activities recorded in the 7-day physical activity diaries were categorised by researcher into sleeping, inactive, and active activities, and then inactive and active activities were time matched with the HR-monitoring data collected during waking hours. The mean value of HR for inactive and active categories was calculated and used to determine corresponding $\dot{V}O_2$ and $\dot{V}CO_2$ using the coefficients produced from the relationship between HR-$\dot{V}O_2$ and HR-$\dot{V}CO_2$ relevant to inactive and active activities (Moon and Bute, 1996). The rate of EE of inactive and active activities was then calculated by indirect calorimetry (Frayn and Macdonald, 1997). TEE was calculated as the sum of activity EE (AEE), which included EE of all active activities except EE of exercise sessions, sedentary EE (SEDEE), and sleeping EE (SEE), which was defined as 95% of RMR (Goldberg et al., 1988). Gross ExEE was calculated using coefficients produced from the relationship between HR-$\dot{V}O_2$ and HR-$\dot{V}CO_2$ obtained during the submaximal test. Net ExEE was calculated by subtracting RMR equivalent for the exercise time from gross ExEE.

4.2.8 Measurement of energy intake

During the week leading to the exercise programme and during week 8, participants were instructed to keep a food diary (Appendix VII) for 7 consecutive days, which involved weighing all food and drink consumed on electronic scales and recording the weight and time of consumption in the diary (Bingham, 1987). Instructions were provided in addition to a visual demonstration by the researcher to show how to use the scales and the diary. The participants were advised to maintain their normal dietary intake. The Diet 5 computer software package (Diet 5, Robert Gordon University, Aberdeen, UK) was then used to analyse the food diaries and to determine macronutrient and micronutrient intake for each participant.

4.2.9 Classification of participants as responders and nonresponders

Change in body mass in response to the exercise training intervention is the sum of change in lean mass and change in fat mass. As the energy density of fat is 39.4 $MJ \cdot kg^{-1}$ and the energy density of lean tissue is 3.7 $MJ \cdot kg^{-1}$ (Elia, 2003), the energy imbalance associated with change in body mass (assuming no change in bone mass) is given by:

$$\Delta\text{Energy balance (MJ)} = \Delta\text{fat mass (kg)} \times 39.4 + \Delta\text{fat free mass (kg)} \times 3.7$$

Thus;

$$\Delta\text{fat mass (kg)} = (\Delta\text{Energy balance (MJ)} - \Delta\text{fat free mass (kg)} \times 3.7)/ 39.4$$

Thus, the expected change in fat mass in response to the exercise training programme can be calculated from the total net ExEE (ΔEnergy balance) and the change in fat-free mass. A comparison of predicted fat loss with actual fat loss was used to determine the extent to which compensation had occurred. Participants achieving less than predicted

fat loss were classified as “nonresponders”, and those achieving more than or equal to their predicted fat loss were classified as “responders”.

4.2.10 Statistical analysis and power calculations

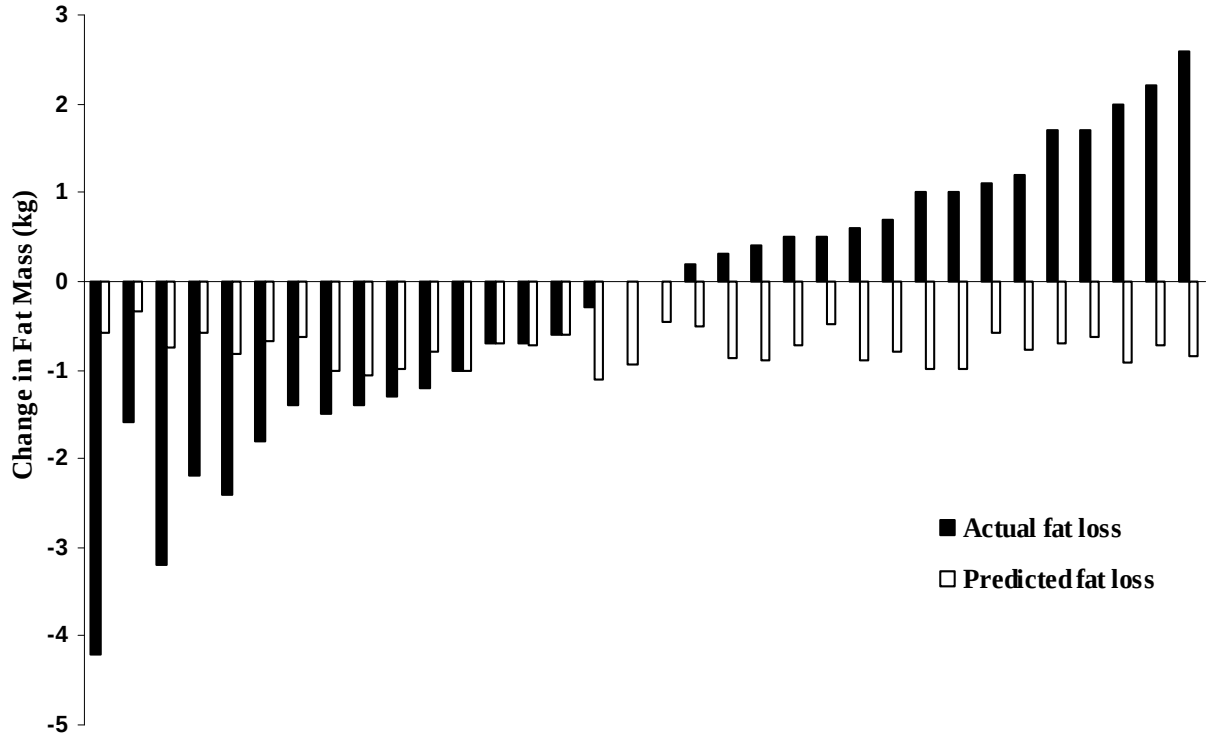
Statistical analysis was performed using Statistica (Version 6.0; StatSoft Inc., Tulsa, OK). Data were tested for normality using the Anderson–Darling test before statistical analysis, and those with distribution significantly different from normal were logarithmically transformed. Data are presented as mean ± SEM, unless otherwise stated. Differences between the two groups at baseline were compared using unpaired t-tests. Changes in all variables from baseline to post intervention assessment were compared by two-way ANOVA (group x time) with repeated measures on the factor “time”. The group x time interaction term was used to determine whether subjects from the group classified as responders and from the group classified as nonresponders responded differently to the intervention, and a *post hoc* Tukey test was used to identify changes within groups. Univariate and multivariate regression analyses were performed to determine whether behavioural compensatory factors (i.e., TEE, AEE, SEDEE, SEE, and energy intake) were significant predictors of the extent of change in fat mass over the entire group of responders and nonresponders combined. Chi-square analysis was performed to determine whether exercise pattern influenced the distribution of responders and nonresponders. The AEE was 4.6 ± 1.7 $MJ \cdot d^{-1}$ at base line (week 0) and 4.4 ± 1.3 $MJ \cdot d^{-1}$ at the end of exercise programme (week 8), and the SD for the difference in AEE between week 8 and week 0 was 1.8 $MJ \cdot d^{-1}$. On the basis of these

data, the present study with 11 responders and 23 nonresponders had sufficient statistical power to detect a difference of 0.9 $MJ \cdot d^{-1}$ in AEE change with 85% power.

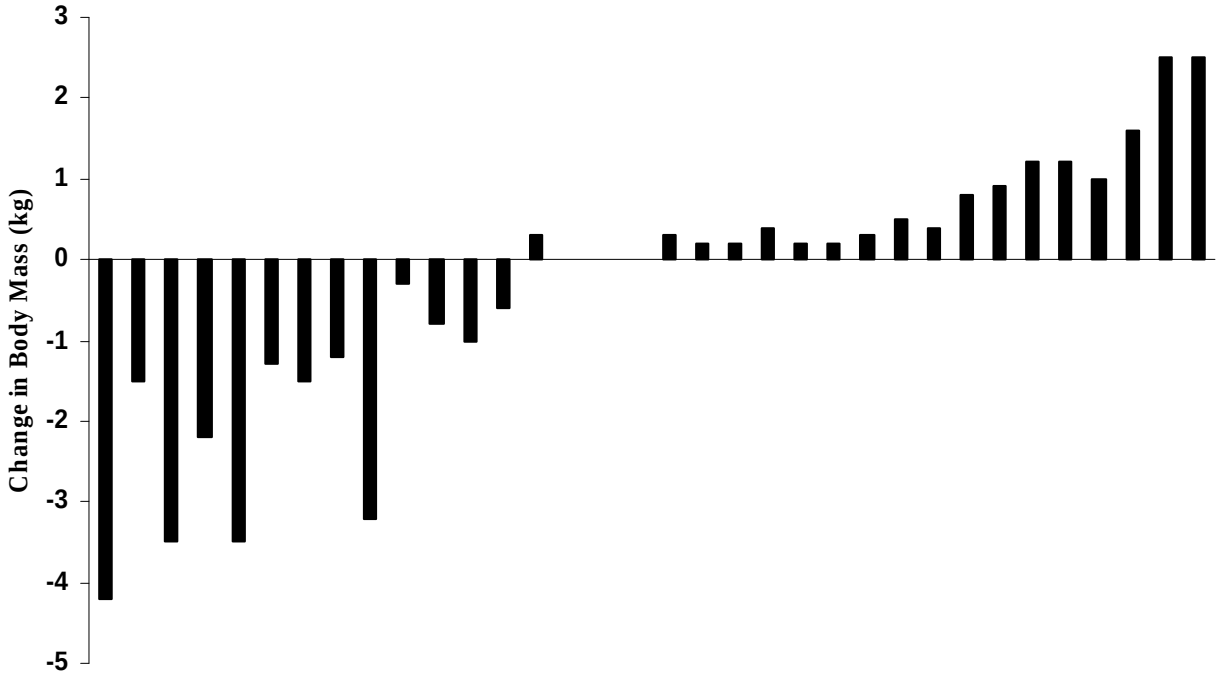
4.3 Results

Compliance with the exercise intervention was 100%, with all participants completing 1200 minutes of supervised exercise over the 8-week exercise intervention. Participants expended 30.2 ± 12.6 MJ and thus were predicted to achieve a body fat loss of 0.8 ± 0.2 kg. However, when the group was considered as a whole, there was no significant change in body fat (-0.0 ± 0.2 kg) over the course of the intervention (Table 4.2). Further examination of the data revealed large individual variability in body fat changes ranging from -3.2 to +2.6 kg (Figure 4.1, A). Eleven of the participants lost more than or equal to their predicted fat loss and were classified as responders, whereas 23 of them lost less than their predicted fat loss and were classified as nonresponders (Figure 4.1, A). Individual body mass (kg) and fat-free mass (kg) change is shown in Figure B and C respectively. There were no differences in body fat loss between participants assigned to exercise pattern A and pattern B (pattern A = -0.25 ± 0.40 kg, pattern B = 0.14 ± 0.33 kg; ANOVA, df = 1, F-ratio = 0.573, p = 0.45 for interaction), and the pattern of exercise did not significantly influence the distribution of responders and nonresponders (pattern A, 11 nonresponders and 7 responders; pattern B, 12 nonresponders and 4 responders; chi-square, p = 0.39).

A.


Change in Fat Mass (kg)
3
2
1
0
-1
-2
-3
-4
-5
Actual fat loss
Predicted fat loss

B.


Change in Body Mass (kg)
3
2
1
0
-1
-2
-3
-4
-5

C.

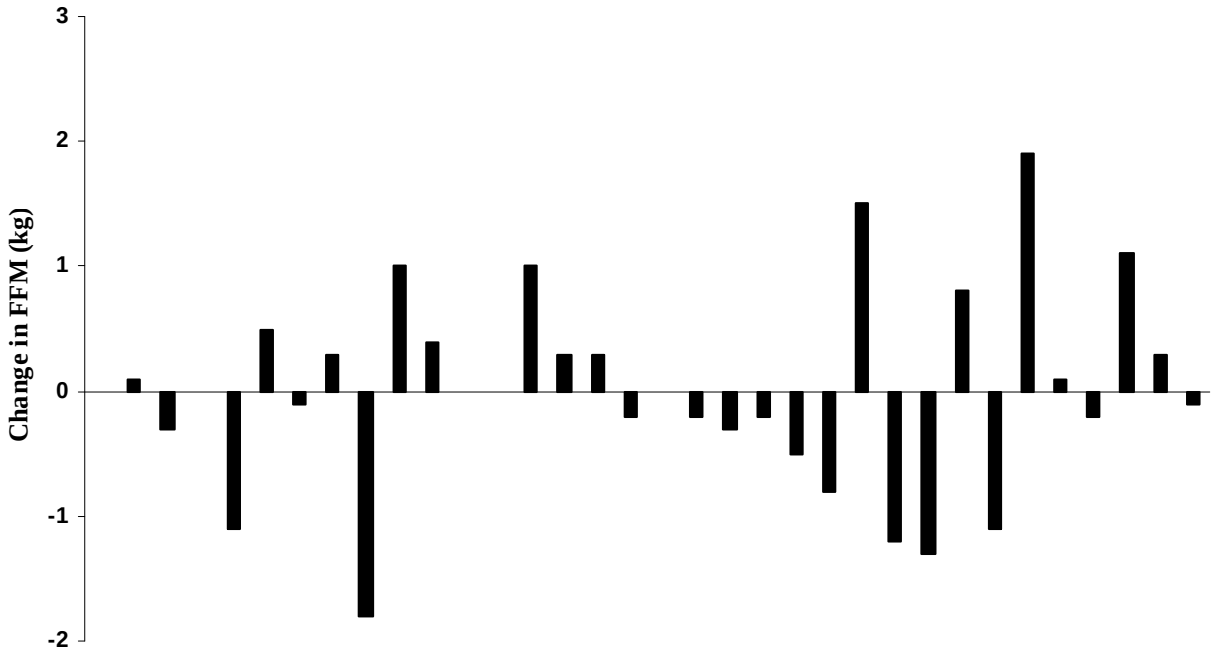


Figure 4.1 Individual predicted and actual change in body fat mass (A), individual actual body mass change (B) and individual actual fat-free mass change (C). Each pair of histograms (A) represents one individual. Participants who achieved less than predicted fat loss were classified as nonresponders, and those who achieved more than or equal to their predicted fat loss were classified as responders.

There were no significant differences in any of the measured baseline variables between responders and nonresponders (Table 4.1). By definition, body fat responses to exercise programme differed significantly between responders and nonresponders, with responders reducing (by 5.6%) and nonresponders increasing (by 1.9%) body fat (df = 1, F-ratio = 45.03, $p < 0.0005$ for interaction) (Table 4.2). Waist circumference decreased by 4.0% for the group as a whole ($p < 0.01$), with no difference between responders and nonresponders. Maximal oxygen uptake increased by 35% (df = 1, F-ratio = 70.61, $p < 0.0005$ for main effect), and $\dot{V}O_2$ at LT increased by 12% (df = 1, F-ratio = 5.376, $p = 0.028$ for main effect) in the group as a whole, with no difference between responders and nonresponders. Exercise training had no effect on RMR (Table 4.2).

Table 4.1 Subject characteristics at baseline for the whole group, responders (n=11) and nonresponders (n=23). Values are mean ± SD.

	Whole Group	responders	nonresponders
Age (years)	31.7 ± 8.1	34.0 ± 6.9	30.7 ± 8.6
Body mass* (kg)	78.9 ± 13.2	75.7 ± 6.8	80.5 ± 15.3
BMI* ($kg \cdot m^{-2}$)	29.3 ± 4.4	28.2 ± 2.0	29.9 ± 5.1
Fat mass* (kg)	31.7 ± 9.6	30.0 ± 5.2	32.4 ± 10.8
Waist circumference* (cm)	91.3 ± 10.3	91.2 ± 6.8	91.3 ± 11.6
TEE ($MJ \cdot d^{-1}$)	9.43 ± 1.66	8.50 ± 0.91	9.80 ± 1.76
AEE ($MJ \cdot d^{-1}$)	4.59 ± 1.72	3.98 ± 0.53	4.83 ± 1.97
SEDEE ($MJ \cdot d^{-1}$)	2.77 ± 0.91	2.50 ± 0.79	2.88 ± 0.95

SEE ($MJ \cdot d^{-1}$)	2.12 ± 0.41	2.03 ± 0.18	2.16 ± 0.47
RMR* ($MJ \cdot d^{-1}$)	5.95 ± 0.71	5.70 ± 0.46	6.05 ± 0.78
$\dot{V}O_{2max}$ ($l \cdot min^{-1}$)	2.07 ± 0.38	2.06 ± 0.33	2.08 ± 0.40
$\dot{V}O_2$ at LT ($l \cdot min^{-1}$)	1.36 ± 0.24	1.32 ± 0.22	1.41 ± 0.24
Energy intake ($MJ \cdot d^{-1}$)	8.31 ± 2.13	7.95 ± 1.96	8.45 ± 2.22
Fat intake ($MJ \cdot d^{-1}$)	2.79 ± 0.71	2.73 ± 0.60	2.82 ± 0.76
Carbohydrate intake ($MJ \cdot d^{-1}$)	4.17 ± 1.36	3.98 ± 1.22	4.25 ± 1.44
Protein intake ($MJ \cdot d^{-1}$)	1.34 ± 0.46	1.25 ± 0.29	1.38 ± 0.49
Alcohol ($MJ \cdot d^{-1}$)	0.11 ± 0.03	0.15 ± 0.04	0.07 ± 0.02

* statistical analysis performed on logarithmically transformed data.

Abbreviations. BMI, body mass index; TEE, total energy expenditure; AEE, activity energy expenditure; SEDEE, sedentary energy expenditure, SEE, sleeping energy expenditure; RMR, resting metabolic rate; $\dot{V}O_{2max}$, maximal oxygen consumption; LT, lactate threshold.

Table 4.2 Responses to exercise programme for the whole group, responders (n=11) and nonresponders (n=23). Values are mean ± SEM.

	Whole Group	responders	nonresponders
Body mass* (kg)	-0.15 ± 0.28	-1.85 ± 0.46 [a]	0.65 ± 0.20 [a,b]
BMI* ($kg \cdot m^{-2}$)	-0.05 ± 0.11	-0.65 ± 0.22 [a]	0.23 ± 0.07 [b]
Fat mass* (kg)	-0.04 ± 0.24	-1.75 ± 0.19 [a]	0.62 ± 0.20 [a, b]
Waist circumference* (cm)	-3.66 ± 0.44 [a]	-4.02 ± 0.76 [a]	-3.52 ± 0.55 [a]
RMR ($MJ \cdot d^{-1}$)	0.15 ± 0.08	0.09 ± 0.17	0.17 ± 0.09

$\dot{V}O_{2max}$ ($l \cdot min^{-1}$)	0.74 ± 0.07 [a]	0.77± 0.10 [a]	0.72 ± 0.15 [a]
$\dot{V}O_2$ at LT ($l \cdot min^{-1}$)	0.17 ± 0.07 [a]	0.24 ± 0.12 [a]	0.14 ± 0.09 [a]
Energy intake ($MJ \cdot d^{-1}$)	0.98 ± 0.43 [a]	0.86 ± 0.75	1.03 ± 0.53
Fat intake ($MJ \cdot d^{-1}$)	0.35 ± 0.15	0.17 ± 0.22	0.43 ± 0.19
Carbohydrate intake ($MJ \cdot d^{-1}$)	0.33 ± 0.26	0.35 ± 0.51	0.33 ± 0.30
Protein intake ($MJ \cdot d^{-1}$)	0.25 ± 0.11	0.14 ± 0.22	0.29 ± 0.13
Alcohol intake ($MJ \cdot d^{-1}$)	0.02 ± 0.00	0.03 ± 0.00	0.01 ± 0.0

[a] significant difference from baseline, $p < 0.05$. [b] significant difference for change between groups, $p < 0.05$.
* statistical analysis performed on logarithmically transformed data.

Abbreviations. BMI, body mass index; RMR, resting metabolic rate; $\dot{V}O_{2max}$, maximal oxygen consumption; LT, lactate threshold.

Over the 8 weeks of the exercise programme, responders and nonresponders expended a similar amount of energy (responders = 28.55 ± 2.14 MJ, nonresponders = 30.29 ± 1.76 MJ, df = 1, F-ratio = 0.032, p = 0.86). Although daily TEE increased by 0.62 ± 0.30 MJ (df = 1, F-ratio = 7.101, p = 0.012 for main effect) in the group as a whole, the increase in TEE tended to be higher in responders than that in nonresponders (responders = +1.44 ± 0.49 MJ, nonresponders = +0.29 ± 0.36 MJ, df = 1, F-ratio = 3.328, p = 0.078 for interaction) (Figure 4.2). Changes in daily AEE, reflecting changes in physical activity outside exercise sessions, were significantly different between groups and differed in direction (responders = +0.79 ± 0.50 MJ, nonresponders = -0.62 ± 0.39 MJ, df = 1, F-ratio = 4.347, p = 0.046 for interaction) (Figure 4.2) but did not differ according to exercise pattern (pattern A = 0.06 ± 0.45 MJ, pattern B = -0.47 ± 0.49 MJ, df = 1, F-ratio = 0.636, p = 0.43 for interaction). There were no differences between responders and

nonresponders for changes in SEDEE (responders = -0.32 ± 0.31 MJ, nonresponders = -0.13 ± 0.32 MJ) and SEE (responders = 0.05 ± 0.09 MJ, nonresponders = 0.07 ± 0.05 MJ).

In the group as a whole, the exercise programme induced a significant ($p < 0.05$) increase in energy intake by 9.7%, although changes in the individual macronutrients (carbohydrate, protein, and fat) did not achieve statistical significance. There were no significant differences between responders and nonresponders in energy, fat, carbohydrate, or protein intake (Table 2). Six of 11 participants in the group of responders and 9 of 23 participants in the group of nonresponders reported energy intakes of less than 1.3 x RMR through the 8 weeks of the intervention. This proportion did not differ significantly between the responder and the nonresponder groups (chi-square, $p = 0.40$).

In both univariate and multivariate regression analyses, change in AEE was the only significant behavioural predictor of change in fat mass ($r = -0.36$, $p = 0.045$), explaining 13% of the variance of change in fat mass in response to the intervention.

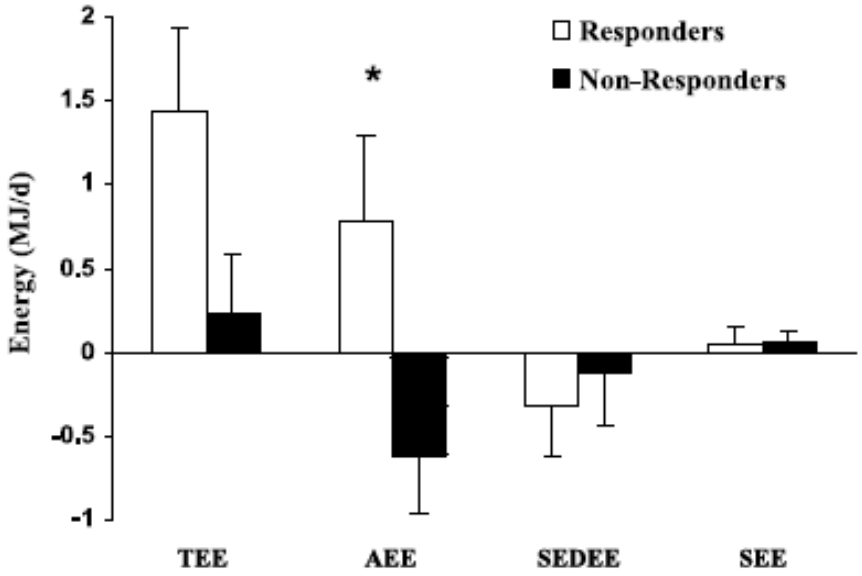


Figure 4.2 Exercise-induced changes in daily total energy expenditure (TEE), activity energy expenditure (AEE) calculated as EE of all active activities except exercise EE (ExEE), sedentary energy expenditure (SEDEE), and sleeping energy expenditure (SEE) in responders and nonresponders.

* significant ($p < 0.05$) difference for change between groups.

4.4 Discussion

The main finding of this study was that individual variability in body weight and fat changes in overweight healthy women in response to a supervised and well-controlled exercise programme is, at least in part, related to individual differences in compensatory changes in EE of physical activity outside exercise sessions. In addition to the evidence that overweight individuals who experience a lower than predicted weight loss are compensating by an increase in energy intake (King et al., 2008), these data suggest that

success of exercise programmes in relation to body fat loss could conceivably be increased by the employment of strategies directed toward the prevention of exercise-induced compensatory behaviours.

Although previous evidence suggests that compensatory reduction in physical activity in nonexercise time may serve as a barrier to exercise-induced body mass and body fat loss (King et al., 2007; Donnelly et al., 2005; Stubbs et al., 2002; Goran and Poehlman 1992), this was the first study aiming to examine whether direction and extent of change in this compensatory behaviour differ between individuals and thus contribute to the interindividual variability seen in body mass and body fat changes during exercise interventions (King et al., 2008; King et al., 2007). We found that the change in AEE, which included EE of all active activities except EE of exercise intervention, was significantly different between responders, that is, those who achieved more than or equal to their predicted fat loss, and nonresponders, that is, those who lost less than predicted fat loss. Indeed, in comparison to the AEE at baseline, the daily AEE measured during the final week of exercise programme decreased by approximately 0.62 MJ in nonresponders and increased by 0.79 MJ in responders. Furthermore, change in AEE was a significant predictor of change in fat mass for the group as a whole. Thus, our data indicate that lower than predicted weight and body fat loss seen in nonresponders can be attributed, at least in part, to a reduction in physical activity outside exercise sessions and implies that direction of the AEE response may be different between those who achieve and those who do not achieve body fat loss.

There is a widely accepted notion that during exercise programmes, the exercise-induced energy deficit at some critical point triggers an increase in energy intake (Melzer et al., 2005). However, the recent study of King et al., (2008), investigating mechanisms responsible for individual variability in body mass and body fat changes during exercise programmes in overweight individuals and measuring energy intake changes from *ad libitum* lunch and dinner meals, reported that over the course of exercise intervention, some of the participants increased and others decreased their energy intake and that differences in energy intake changes contributed to the individual variability in body mass and body fat loss. In contrast, the current study found that the exercise-induced change in energy intake was not significantly different between those who lost less and those who lost more than predicted body fat. It is appreciated that energy intake assessment using the 7-day weighed intake measurements used in the present study may be less precise than the measurements made in the study of King et al., (2008), and as is the case in all studies using weighed food records, comparison of energy intake between baseline and during last week of exercise intervention could potentially be confounded by inaccuracies in data collection (Hill and Davies, 2001) and underreporting (Goris et al., 2000). Indeed, consistent with the existing evidence that, in obese individuals, underreporting commonly lies within the range of 20%– 50% (Hise et al., 2002; Goris et al., 2000), it was found that 40% of the participant of this study reported energy intake less than RMR x 1.3. On the other hand, it is important to note that in the present study, the volume of exercise was substantially lower in comparison to the exercise volume in the study of King et al., (2008) (~4 vs ~10 $MJ \cdot wk^{-1}$). Thus, it is possible that energy intake compensatory responses to exercise may be influenced by extent of the energy

balance perturbation and that that lower ExEE in the present study was below the threshold required for a compensatory response. This suggestion requires further investigation, and findings of such studies may contribute to the design of the exercise programmes that provide more favourable body fat and body weight changes.

Although the capacity of behavioural responses to compensate for disturbances in energy balance is expected to be more powerful than metabolic responses (King et al., 2007), it is appreciated that lower than expected body weight and fat loss seen in this and other supervised and controlled exercise training studies (King et al., 2008) may be explained not only by behavioural but also by metabolic compensatory responses. For example, it has been reported that in men residing at an isolated experimental station in a highly controlled environment, imposition of an exercise-induced energy deficit of 4.2 $MJ \cdot d^{-1}$ for 84 days, with constant energy intake, led to reductions in body weight ranging from 3 to 12 kg, which is unlikely to be fully explained by differences in compensatory activity between participants (Bouchard et al., 1990). One metabolic factor that may contribute to the difference in response to exercise training is change in RMR. However, in agreement with the study of King et al., (2008), the current study found that changes in RMR between the start and the end of the intervention did not differ between responder and nonresponder groups. The identification and the characterisation of metabolic compensatory responses require further research.

In this study, overweight and obese but otherwise healthy women undertook an exercise training programme on the basis of current exercise recommendations (Haskell et al.,

2007), exercising for 150 min·wk·$^{-1}$ at exercise intensity corresponding HR ranging from 135 to 145 beats·min^{-1}, which corresponded to 72%–77% of the age-predicted HR_{max}. In participants who did not reduce physical activity outside exercise sessions, this volume of exercise led to a significant reduction in adiposity. It is important to note that most of the participants, despite having quite low initial fitness levels, found this volume of exercise to be achievable and enjoyable. Therefore, when combined with an advice on how to eliminate behavioural compensatory responses, this level of exercise can be recommended for the reduction of overweight and obesity.

The data obtained in this study demonstrate that regardless of the direction and extent of body fat changes, all participants experienced health benefits as a result of the exercise programme. It was found that waist circumference was reduced by approximately 4 cm in both responders and nonresponders. This suggests that even under conditions of no body fat loss, exercise may induce favourable fat redistribution. This is of great importance because increased abdominal adiposity is thought to reflect visceral fat surrounding the internal organs (Minderico et al., 2008), which can pose a high risk of chronic disease such as heart disease and type 2 diabetes (Despres et al., 2001). In addition, both groups benefited from the exercise programme by increasing their $\dot{V}O_{2max}$ by approximately 0.74 l·min^{-1}, thus improving their cardiorespiratory fitness, another important predictor of good health (Gill and Malkova, 2006).

In the present study, the group as a whole did not lose a significant amount of body fat in response to the exercise intervention, which included 150 minutes of moderate-intensity

exercise per week. This contrasts somewhat with a recent study from Church et al., (2009), who in a 6-month trial found that sedentary, overweight postmenopausal women who undertook ~72 or ~136 minutes of exercise per week had actual weight losses that did not differ significantly from predicted weight losses, whereas women who undertook ~194 minutes of exercise per week lost less weight than predicted, suggesting that whether compensation occurs is related to exercise dose. No differences in step counts outside of exercise were observed between the three exercise doses (Church et al., 2009). However, it is important to consider that over 50% of women undertaking ~136 minutes of exercise lost less weight than predicted in that study, indicating that the extent of compensation differed markedly between individuals at any given exercise dose (Church et al., 2009). In the current study of relatively young, overweight or obese women, individual differences in changes in AEE explained 13% of the variance in the extent of exercise-induced fat loss; however, King et al., (2008) found that dietary compensation contributed to individual variability in weight loss on a group of middle-aged men and women—an effect that we did not see in the present study. Thus, it appears that both the mechanisms and the magnitude of behavioural compensation to induced exercise differ substantially between individuals, and this information is lost when group mean values are considered. This highlights the importance of considering data at the individual rather than the group level to obtain a more complete understanding of factors influencing the extent of fat loss in response to exercise.

The main limitations to this study, which are common to the majority of reports in this field, relate to the measurement of behavioural compensation variables. Issues related to

the potential underreporting of dietary intake (Hise et al., 2002; Goris et al., 2000) have been highlighted above, but it is important also to recognise that the extent of underreporting appears to be relatively consistent within an individual (Black and Cole, 2001), implying that differences in dietary intake between two observation points (e.g., changes from intake from baseline to post intervention) are likely to be determined with greater accuracy than absolute dietary intakes at a single time point. Thus, the repeated-measures design in the present study may have attenuated the magnitude of this potential error. There is no gold standard technique for assessing components of EE in free-living individuals because the gold standard method for measurement of TEE—the DLW method— does not allow for calculation of separate activity components. We used a combination of HR monitoring and physical activity diaries to determine components of EE without the exercise intervention. This approach has been shown to have greater accuracy than HR monitoring alone, agreeing well with room calorimetry measurements (Moon and Bute, 1996), but the use of a self-report diary for classification of active and inactive domains could conceivably introduce errors. In addition, the study at 8 week was relatively short term, and further investigations are needed to determine whether differences in physical activity compensation are predictive of the extent of fat loss in response to an exercise intervention over the longer term. Further study is also needed to determine the effects of different exercise doses on behavioural compensation at the individual level. A final limitation of the study relates to statistical power. Because it was not possible to predict the number of participants who would be classed as responders and nonresponders until completion of the study, it was difficult to perform an *a priori* power calculation. A retrospective power calculation indicated that the study

had sufficient power to detect a difference in AEE between the responder and the nonresponder groups; however, the study was slightly underpowered to reveal a significant difference in TEE between the groups: the tendency for a difference in TEE may have become significant with a larger number of participants.

In conclusion, these findings confirm that there is a large degree of interindividual variability in body fat loss in response to an exercise training intervention and indicated that, in overweight women, compensatory reductions in EE of physical activity outside exercise intervention can contribute to the failure of exercise to successfully induce fat loss.

Chapter 5: Effects of two different exercise patterns on physical, fitness and metabolic variables in overweight women

5.1 Introduction

Despite the clear evidence that undertaking physical activity is associated with reduced risk of many diseases (Warburton et al., 2006) participation rates remain low (CDC, 2008) with more than two-thirds of European and US populations undertaking less physical activity than is currently recommended (Flegal et al., 2010; Bauman et al., 2009; European Commision, 2006). Current UK physical activity guidelines recommend that adults undertake at least 30 minutes of moderate physical activity on 5 or more days of the week (CMO, 2004); with US guidelines recommending at least 30 minutes of moderate physical activity on 5 days of the week, at least 20 minutes of vigorous aerobic activity on three days of the week, or a combination of the two (Haskell et al., 2007). Thus, if individuals choose to engage in moderate-intensity activities, they must undertake physical activity on most days of the week to achieve the guidelines as currently stated. Lack of time is often cited as a barrier to undertaking physical activity in developed countries (Reichert et al., 2007; Stutts, 2002; Zunft et al., 1999), and thus, performing exercise on fewer days per week might be a more attractive option for those who find it difficult to find time to be active on most days. However, it is not currently clear whether undertaking less frequent, but longer duration exercise sessions of moderate-intensity, would elicit similar metabolic health benefits as the 5 x 30 minute pattern recommended in current guidelines.

There is some evidence to suggest that longer duration, less frequent exercise may be at least as beneficial as daily exercise. In a single-leg exercise training model in which one leg trained for 2 hours every second day and the other trained for 1 hour every day, Hansen and co-workers (2005) found greater improvements in exercise capacity and oxidative enzymes activity in the leg which undertook less frequent exercise. Thus, it is not unreasonable to hypothesise that undertaking the volume of physical activity recommended in physical activity guidelines, in longer, less frequent sessions, would be at least as beneficial as the 5 x 30 minute pattern.

The aim of this study was therefore to compare the effects on fitness and metabolic health outcomes of two 8-week supervised exercise programmes each providing at total 150 minutes of moderate-intensity exercise per week, in the form of 30 minutes on 5 days of the week or 75 minutes on two days of the week. Sedentary overweight and obese women were chosen for study as they form a key group who would benefit from a moderate-intensity exercise intervention.

5.2 Methods

5.2.1 Participants

Initially thirty-six overweight or obese women were recruited, of which thirty-four completed the 8-week exercise programme. One participant dropped from the study due to unrelated health problems and another due to personal issues. Three quarters of the participants were the same individuals as in Chapter 4. Baseline physical and fitness

characteristics are shown in Table 5.1. Exclusion criteria, recruitment and ethical approval process are described in detail in section 2.1 of General Methods.

5.2.2 Study design

Participants performed an 8-week supervised exercise programme, undertaking 150 minutes of exercise per week at cycling intensities determined by the individual LT (see below for details of intensity) (Figure 5.1). Participants were randomly assigned to either a long exercise bouts group (LB) or a short exercise bouts group (SB). Prior the first exercise session and 16-18 and 60-62 hours after the final exercise session measurements of body composition, blood pressure, RMR, respiratory exchange ratio (RER) (see General Methods, section 2.2) and waist circumference (see section 4.2.6) were obtained and fasting blood samples were collected. Blood samples were used for the measurements of plasma insulin, sVCAM-1, plasma glucose, TG, total, LDL, and HDL cholesterol and CRP concentrations (see General Methods, section 2.4). Lactate threshold was established and $\dot{V}O_2max$ was predicted (see General Methods, section 2.3) before, during 4th week and after the end of the exercise programme.

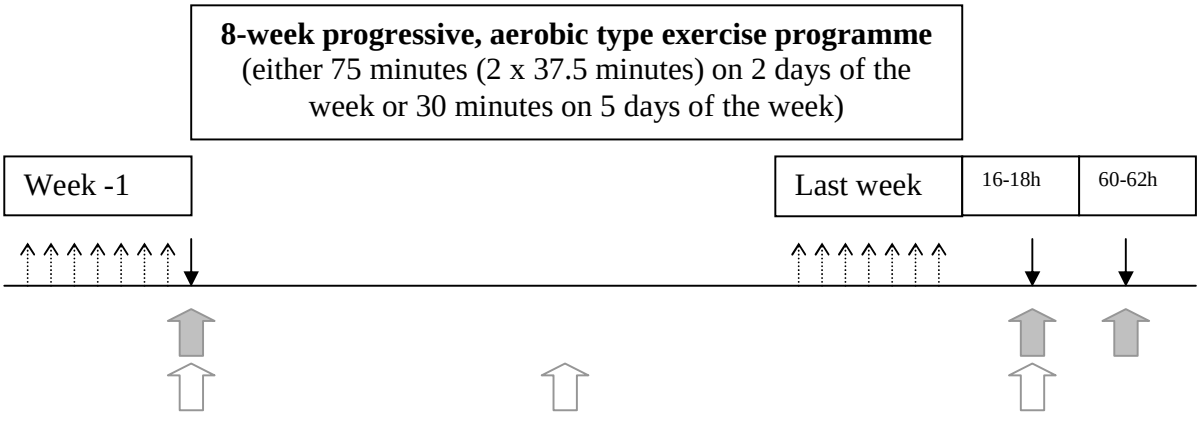
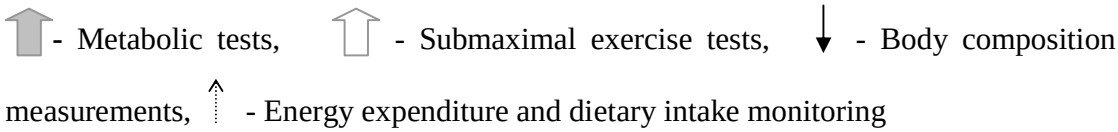


Figure 5.1 Schematic representation of the study design. The arrows indicate the days when the tests were done:



5.2.3 Exercise intervention

All participants undertook 150 minutes of supervised exercise per week. Participants in the LB exercise group exercised for 75 minutes twice per week (LB, n=16) and participants in the SB exercise group exercised for 30 minutes five times per week (SB, n=18). Participants in the LB group were permitted one 5-minute break midway through each exercise session. Exercise sessions were all performed under laboratory conditions on friction-braked cycle ergometers (Ergomedic 873, Monark, Sweden) at least 3 hours postprandially and at a time convenient for participants under the supervision of a researcher. The workload was individually set at 90% of the LT for the first two weeks followed by 95% of the LT for the next two weeks. Lactate threshold was reassessed after 4 weeks of the intervention; exercise intensity was 90% of the new LT for the next 2 weeks and 95% of this value for the final 2 weeks of the programme. The prescribed weekly external workload corresponded to 0.69 ± 0.07 MJ in LB group and 0.75 ± 0.05 MJ in SB group. During exercise sessions HR was continuously recorded through short-range telemetry HR monitors (Polar S610i, Polar Electro Oy, Kempele, Finland) to ensure that individuals were working at a consistent and safe level and then HR data

were downloaded to a University computer through an infrared port using Polar software (Polar Electro Oy, Kempele, Finland) for further analysis.

5.2.4 Blood collection

Blood collection took place in the metabolic investigation suite (Figure 2.1) by a qualified and experienced person who drew 7.5 ml of blood through a small butterfly. All samples were collected into a 7.5ml ethylenediamine tetra-acetic acid (EDTA) Vacutainer™ tube (BD Vacutainer Systems, Plymouth, UK) and were placed on ice prior centrifugation at 4ºC, 3000 rpm for 15 minutes. Plasma was aspirated after centrifugation using a disposable plastic Pasteur pipette. Fasting plasma was dispensed in 6-8 0.5 ml aliquots into labeled 2 ml eppendorfs (Alpha Laboratories Ltd, UK), and frozen at -80ºC until analysis.

5.2.5 Statistical analysis and power calculation

Statistical analysis was performed using Statistica (version 6.0, StaSoft Inc., Oklahoma). Data were tested using the Anderson-Darling normality test before statistical analysis and those with distribution significantly different from normal were logarithmically transformed. Results are shown as Mean ± SEM unless otherwise stated. The $HOMA_{IR}$, as described in section 2.4 of General Methods, was used as a validated index of insulin resistance (Matthews et al., 1985). Differences between the two groups at baseline were checked using unpaired t-tests. Changes in all variables from baseline to post-intervention assessment were compared by 2-way ANOVA (group x time) with repeated measures on the ‘time’ factor. The group x time interaction term was used to determine

whether the LB group and the SB group individuals responded differently to the exercise programme. The level of significance was accepted at $p < 0.05$. An *a priori* power calculation based on data available from other studies conducted in our laboratory indicated that 15 subjects per group would be needed to detect a 10% difference in effect of exercise on $HOMA_{IR}$ between groups, with 85% power at $p < 0.05$, assuming an SD of 0.16 units for change in $HOMA_{IR}$, based on data from a similar study.

5.3 Results

5.3.1 Compliance to exercise intervention

Exercise intervention compliance was 100%, with all participants completing 1200 minutes of supervised exercise over the 8-week exercise intervention. The LB group completed 16 sessions at HR of 127 ± 1 beat·min^{-1} with a total external workload of 5.64 ± 0.34 MJ, and the SB group completed 40 sessions at HR of 126 ± 1 beat·min^{-1} with a total external workload of 5.83 ± 0.23 MJ. Exercise HR and external work done did not differ between groups.

5.3.2 Baseline measurements and exercise-induced changes

Physical and fitness variables at baseline and post-intervention are shown in Table 5.1. At baseline physical and metabolic characteristics between LB and SB were not significantly different. Exercising for 8 weeks significantly reduced waist circumference (by 3.9 ± 0.5%, p= 0.001) and diastolic blood pressure (by 3.8 ± 1.7%, p=0.01) and increased $\dot{V}O_2$ max (by 35.4 ± 3.9%, p= 0.001), and workload at which LT was achieved (by 30.8 ± 3.4%, p= 0.001) but had no significant impact on body mass, BMI, fat mass

percentage body fat and fat free mass. The group x time interaction was not significant for any of these factors, indicating that responses to exercise training did not differ between the SB and LB groups.

Metabolic variables at baseline and post-intervention (16-18 hours after the final exercise session) are shown in Table 5.2. There were no differences between groups at baseline in any of these variables. Exercising for 8 weeks significantly increased RMR (by 3.4 ± 1.3%, p= 0.02) and significantly decreased insulin concentration (by 7.1 ± 8.0%, p= 0.03) and $HOMA_{IR}$ (by 9.1 ± 6.5%, p= 0.02). Plasma TG concentrations tended to be lower (p= 0.07) at the end of the exercise programmes but concentration of total-, HDL- and LDL-cholesterol, CRP and sVCAM-1 were not significantly different from baseline. Responses to exercise training did not differ between the SB and LB groups for any of the metabolic variables.

5.3.3 Acute versus chronic effects of the exercise intervention

There were no significant differences between measurements made at 60-62 hours after the last exercise session and baseline or 16-18 hours after the last exercise session for any of the measured metabolic variables as glucose (LB, 4.91 ± 0.13; SB, 5.32 ± 0.11 $mmol \cdot l^{-1}$), insulin (LB, 8.84 ± 1.08; SB, 9.02 ± 0.94 $mIU \cdot l^{-1}$), $HOMA_{IR}$ (LB, 1.92 ± 0.23; SB, 2.36 ± 0.30), HDL (LB, 1.24 ± 0.06; SB, 1.48 ± 0.07 $mmol \cdot l^{-1}$), LDL (LB, 2.63 ± 0.25; SB, 2.84 ± 0.16 $mmol \cdot l^{-1}$), TG (LB, 1.11 ± 0.09; SB, 1.04 ± 0.13 $mmol \cdot l^{-1}$) and CRP (LB, 2.47 ± 0.49; SB, 3.07 ± 0.53 $ng \cdot ml^{-1}$).

Table 5.1 Physical and fitness variables at baseline and post-intervention for the long bouts group and the short bouts group. Values are mean ± SEM.

	Long bouts (n = 16)		**Short bouts (n = 18)**		p-value (exercise effect)	p-value (group x time interaction)
	Baseline	Post-intervention	Baseline	Post-intervention		
Age (years)	32.1 ± 1.8		31.3 ± 2.1			
Body mass* (kg)	81.5 ± 4.1	81.1 ± 4.3	76.7 ± 2.3	76.8 ± 2.5	0.63	0.45
BMI* ($kg \cdot m^{-2}$)	29.7 ± 1.1	29.6 ± 1.2	29.0 ± 1.0	29.0 ± 1.1	0.69	0.51
Fat mass* (kg)	33.8 ± 2.8	33.1 ± 2.9	29.5 ± 1.8	29.7 ± 1.8	0.92	0.15
Body fat (%)	40.4 ± 1.3	39.9 ± 1.3	37.9 ± 1.2	38.1 ± 1.1	0.75	0.07
Fat free mass* (kg)	47.9 ± 1.5	48.0 ± 1.5	46.4 ± 1.1	47.0 ± 0.9	0.39	0.75
Waist circumference* (cm)	94.2 ± 2.7	90.3 ± 2.4	88.5 ± 2.2	85.1 ± 2.2	**0.0001**	0.70
$\dot{V}O_{2max}$ ($l \cdot min^{-1}$)	1.96 ± 0.09	2.72 ± 0.16	2.14 ± 0.10	2.78 ± 0.13	**0.0001**	0.59
Power output at lactate threshold (Watts)	76 ± 5	99 ± 5	82 ± 5	102 ± 5	**0.0001**	0.43
Heart rate at lactate threshold ($beats \cdot min^{-1}$)	137 ± 1	136 ± 1	136 ± 1	135 ± 1	0.32	0.86
Systolic blood pressure (mm Hg)	126 ± 3	121 ± 3	119 ± 3	120 ± 2	0.28	0.20
Diastolic blood pressure (mm Hg)	85 ± 2	79 ± 2	81 ± 2	79.2 ± 1	**0.01**	0.25

*statistical analysis performed on logarithmically transformed data. No significant difference between groups for any values at baseline.

Abbreviations. BMI, body mass index; $\dot{V}O_{2max}$, maximum oxygen uptake.

Table 5.2 Metabolic variables at baseline and post-intervention (16-18 hours) for the long bouts group and the short bouts group. Values are mean ± SEM.

	Long bouts (n = 16)		**Short bouts (n = 18)**		p-value (exercise effect)	p-value (group x time interaction)
	Baseline	Post-intervention	Baseline	Post-intervention		
RMR* ($MJ \cdot day^{-1}$)	5.98 ± 0.21	6.14 ± 0.27	5.83 ± 0.14	6.05 ± 0.10	**0.02**	0.38
RER	0.82 ± 0.02	0.80 ± 0.01	0.83 ± 0.01	0.83 ± 0.02	0.54	0.52
Fat oxidation rate ($g \cdot min^{-1}$)	0.07 ± 0.01	0.07 ± 0.01	0.06 ± 0.01	0.06 ± 0.01	0.35	0.69
Glucose ($mmol \cdot l^{-1}$)	5.06 ± 0.08	4.98 ± 0.12	5.26 ± 0.14	5.34 ± 0.09	0.94	0.32
Insulin* ($mIU \cdot l^{-1}$)	9.19 ± 1.06	7.92 ± 0.88	9.82 ± 0.97	8.88 ± 1.34	**0.03**	0.95
$HOMA_{IR}$*	2.10 ± 0.27	1.78 ± 0.22	2.62 ± 0.32	2.32 ± 0.31	**0.02**	0.88
Total cholesterol* ($mmol \cdot l^{-1}$)	4.33 ± 0.23	4.45 ± 0.25	4.15 ± 0.45	4.06 ± 0.45	0.50	0.84
HDL cholesterol ($mmol \cdot l^{-1}$)	1.28 ± 0.08	1.30 ± 0.07	1.46 ± 0.05	1.46 ± 0.07	0.80	0.68
LDL cholesterol ($mmol \cdot l^{-1}$)	2.56 ± 0.24	2.69 ± 0.22	2.78 ± 0.22	2.86 ± 0.18	0.31	0.79
Triglycerides* ($mmol \cdot l^{-1}$)	1.09 ± 0.11	1.00 ± 0.08	1.06 ± 0.11	0.98 ± 0.11	0.07	0.80
CRP ($ng \cdot ml^{-1}$)	2.52 ± 0.63	2.45 ± 0.60	3.59 ± 1.16	3.01 ± 0.82	0.37	0.48
sVCAM-1 ($ng \cdot ml^{-1}$)	361.1 ± 31.2	344.6 ± 32.1	465.3 ± 34.1	454.0 ± 21.7	0.61	0.92

*statistical analysis performed on logarithmically transformed data. No significant difference between groups for any values at baseline.

Abbreviations. RMR, resting metabolic rate; RER, respiratory exchange ratio; $HOMA_{IR,}$ homeostasis model estimated insulin resistance; HDL, high-density lipoprotein; LDL, low-density lipoprotein; CRP, C-reactive protein; sVCAM-1, soluble vascular cell adhesion molecule-1.

5.4 Discussion

The main finding of this study is that 8-week exercise programmes incorporating 5 x 30 minutes or 2 x 75 minutes of moderate to high intensity exercise per week, induced similar changes in fasting insulin concentrations, $HOMA_{IR}$, RMR, predicted $\dot{V}O_2max$, intensity at which LT was achieved and waist circumference in previously sedentary overweight women. Thus, this data shows that provided the intensity and total volume of exercise are the same, varying frequency and duration of exercise sessions does not influence the magnitude of the physical, fitness and metabolic benefits of exercise. This evidence suggests that individuals can be more flexible in planning their physical activity programmes than is currently suggested by current physical activity guidelines, and provides a viable exercise option for those who struggle to find time to be active on most day of the week.

In the present study 150 minutes of exercise per week for 8 weeks, increased $\dot{V}O_2$ max and LT by 26% and 22%, respectively, reduced insulin resistance by 13% and diastolic blood pressure and waist circumference by approximately 4%. These are substantial differences which are likely to reduce vascular and metabolic disease risk (Zoeller et al., 2007; Gill and Malkova, 2006), and confirm that this volume of exercise is sufficient to elicit these effects in overweight and obese women. In common with a number of other studies (Nassis et al., 2009; Church et al., 2007; Nassis et al., 2005; Hasbum et al., 2005; Duncan et al., 2003), these effects were achieved in the absence of measurable changes in body weight or body fat. Therefore, the findings of this study contribute further to the notion that the pragmatic minimum activity target of 150 minutes of moderate exercise

per week brings health benefits beyond reduction in body mass and body fat. Most importantly, since changes of all listed physical, fitness and metabolic variables were not significantly different between SB and LB groups, the present data suggests that significant and meaningful health benefits of 150 minutes of weekly exercise can be achieved by either exercising for 30 minutes on five days or 75 minutes on two days per week.

Despite exercise induced favourable changes in fitness, insulin sensitivity, blood pressure and waist circumference, there were no substantial changes in other measured cardiovascular disease risk factors such as fasting concentrations of plasma lipids, CRP and VCAM-1. Although the commonly expected change in lipids with exercise is increase in HDL-cholesterol with reduction in total cholesterol, LDL-cholesterol and TG being less frequently observed (Leon and Sanchez, 2001); in the present study exercise induced changes in plasma concentration of plasma lipids were not significant. No change observed in plasma lipids in our study, could be related to the fact that baseline lipid levels were within the clinically normal range (NCEP, 2001), as it is shown that lipid concentration improves favourably mainly in those subjects with the poorest baseline profile (Church et al., 2007; Haskell et al., 1986).

Increased systemic inflammation is considered to be an important adiposity-related factor associated with increased CVD risk (Berg and Scherer, 2005) and circulating concentrations of adhesion molecules, such as VCAM-1, are indicators of endothelial dysfunction related to chronic diseases as atherosclerosis (van der Wal et al., 1992) and

type 2 diabetes (Bluher et al., 2002). The present study found no effect of exercise training on circulating concentrations of CRP – a marker of inflammation – or VCAM-1. This may be due to the exercise programme not being long-term or intensive enough to alter these variables, but our findings of no change in these are in agreement with a number of reports in the literature (Tonjes et al., 2007; Huffman et al., 2006; Hammett et al., 2006; Nassis et al., 2005; Marcell et al., 2005). However, other studies have reported exercise training-induced changes in CRP (Milani et al., 2004) and in VCAM-1 (Tonjes et al., 2007), although the latter was only evident in patients with impaired glucose tolerance and type-2 diabetes and not in normoglycaemic individuals.

Despite being overweight or obese and having quite low initial fitness levels, the women in the LB group were able to complete the 75-minute exercise sessions without any obvious difficulties. This implies that less frequent and longer duration sessions of moderate-intensity exercise are a feasible option for even unfit or overweight individuals who are aiming to increase their physical activity levels to improve their health. It should be noted, however, that in this study all exercise sessions were individually supervised and therefore participants received continuous encouragement and support from researchers. A randomised controlled trial is warranted to determine how adherence to a 2 x 75 minute pattern of exercise would compare to the currently recommended 5 x 30 minute pattern when moderate exercise is conducted in a “real-world” setting.

In conclusion, the findings of the present study show that undertaking 2 x 75 minute exercise sessions per week and 5 x 30 minute exercise sessions per week for 8 weeks elicited similar changes to fitness, insulin resistance, diastolic blood pressure and waist circumference in sedentary overweight and obese women. This suggests that individuals can be flexible in their pattern of exercise throughout the week, undertaking exercise less frequently than recommended in current physical activity for health guidelines, provided the total weekly volume of exercise undertaken is the same. This may be attractive for individuals who find it difficult to undertake physical activity on most days of the week.

Chapter 6: General Discussion

Obesity is a multifactorial condition that occurs as a result of long-term energy imbalance and despite considerable efforts to reduce its prevalence, obesity continues to rise (Ford and Mokdad, 2008). As physical activity is the most variable component of TEE and is well known to modulate risk factors leading to chronic disease, it has long been targeted by interventions to decrease or control body mass as well as to ameliorate metabolic risk. The primary objective of this thesis was to elucidate the extent to which energy balance perturbations induced by exercise influence appetite and compensatory changes in energy intake and/or EE of physical activity outside exercise sessions in overweight and obese women. These effects were studied in response to a single exercise session and in response to an 8-week well structured and supervised exercise programme. The acute exercise study in parallel aimed to investigate how exercise modifies response of metabolic risk factors to *ad libitum* meals consumed several hours after exercise. In addition, this thesis examined changes in the physical, fitness and metabolic variables that occur in response to 8- week moderate intensity exercise programmes with same total duration and total external workload but different frequency and duration of exercise sessions in overweight and obese women.

Current physical activity recommendations suggest that sixty minutes or more per day or approximately 2 MJ expended through exercise would be needed to maximise weight loss or prevent weight gain (Donnelly et al., 2009; Saris et al., 2003; Jakicic et al., 2001). The study presented in Chapter 3 demonstrates that sedentary overweight and obese

women undertaking a single cycling exercise session with EE in line with the amount recommended for weight loss, do not compensate by increasing food intake or appetite measured during four *ad libitum* meals over two consecutive days. These findings agree with the vast majority of literature suggesting that exercise does not stimulate higher appetite and energy intake in the short-term (Blundell et al., 2003). Data of this study also partly confirm physical activity recommendations and suggest that if exercise sessions with EE of approximately 2 MJ are repeated, they are likely to have a significant role for weight loss and/ or weight maintenance in overweight and obese women. In general, this is one of few acute existing exercise studies that are conducted on overweight and obese women aiming to investigate the impact of acute exercise on subsequent energy intake (George et al., 2003; Tsofliou et al., 2003; Kissileff et al., 1990). Most importantly, in contrast to aforementioned studies that were limited in terms of short post-trial observation period, use of one *ad libitum* meal and low ExEE, this is the first study to extend the period of observation over two consecutive days providing in total four *ad libitum* meals and involve higher amount of ExEE conducted on this particular population. However, findings do not eliminate the possibility that compensation does not occur in later post-exercise stages. It is therefore proposed, that future research considers the implementation of longer observation periods after acute exercise, as it is has been previously hypothesised that a critical point exists when energy intake increases to match EE, but this hypothesis has not been fully confirmed (Melzer et al., 2005; Blundell et al., 2003; Blundell and King, 1999).

Although the study presented in Chapter 3 demonstrates that a single exercise session has no influence on appetite and energy intake in response to *ad libitum* meals implying that body mass loss could be achieved by exercise, there is evidence suggesting that exercise programmes without dietary control are not successful in inducing favourable body fat and mass changes (Miller et al., 1997). Many exercise interventions aiming at weight reduction have been proved largely ineffective as actual weight loss of participants does not match the level of predicted and this is mainly attributable to compensation functions (Boutcher and Dunn, 2009; King et al., 2007; Blundell et al., 2003). King et al., 2008 has demonstrated that compensation mechanisms in men and women highly rely on individual differences in energy intake during a 12-week exercise programme. Although King and colleagues (2008) found that the group as a whole lost weight when expended approximately 500 kcal (~ 2 MJ) per day on five days of the week, large individual differences compelled the division of participants to compensators and noncompensators. Energy intake measured by *ad libitum* meals in this study, was found to be the only contributing factor to the interindividual variability in body mass loss, while EE outside the exercise sessions was not measured. In Chapter 4 of this thesis an attempt was made to elucidate if compensatory responses in terms of energy intake and TEE and components such as outside exercise activity, sedentary and sleeping EE are evident, when participants undertake an 8-week exercise programme consisting of 150 minutes of cycling exercise per week according to physical activity recommendations (Haskell et al., 2007; CMO, 2004). Since it could be expected that compensatory responses are gender specific (Stubbs et al., 2002a,b) this study considered compensatory responses to an exercise training programme in overweight

and obese women for the first time. Measurements of body composition, energy intake, TEE and components were taken in overweight and obese women before and during the last week of a structured and supervised 8-week cycling exercise programme. When data were considered as a whole no change in body mass and body fat was evident. However, interindividual variability was large with some women achieving more or equal to the predicted body fat loss and considered "responders", whilst others appeared to have no change or even gained body fat due to compensation for the exercise-induced energy deficit and considered to be "nonresponders". Therefore this study supports the notion that humans participating in exercise intervention studies can be separated into responders and nonresponders and considering data of the group as a whole might be misleading (King et al., 2008; Blundell et al., 2003). In addition, nonresponders were found not to compensate for the energy expended in the exercise programme by increasing energy intake but by decreasing activity EE outside the exercise programme, which finding is in contradiction to previous evidence suggesting that energy intake is the main compensatory mechanism in these individuals (King et al., 2008). However, as in Chapter 4 energy intake was measured by 7-day weighted intake, underreporting reached 40% which is a common finding among obese individuals (Hise et al., 2002; Goris et al., 2000). Thus, the finding that this study indicated no energy intake compensation in nonresponders does not necessarily mean that both energy balance components could not account for the evident interindividual variability. The fall in AEE could be partly explained by lost and substitution time as suggested by Turner et al. (2010). That essentially means that structured exercise reduces the time available for other activity or replaces other activity. However, although this could be somewhat

‘normal’, a group of participants managed to overcome this effect and increase their activity outside exercise sessions. With the existing data it is difficult to conclude whether these beneficial behavioural changes are related to the sympathetic nervous system function, indirect effects of weight loss or improvements in self-efficacy, but they are rather irrelevant to cognitive volitional behavioural changes as no counseling was provided (King et al., 2007) and participants who were seeking to lose weight were not included in the intervention. Future research should arguably focus to the understanding of this particularly interesting finding and decode the mechanism by which some people may increase AEE while participating in an exercise intervention. Overall, these data suggest that success of exercise programmes in relation to body fat loss could conceivably be increased by the employment of strategies directed towards the prevention of exercise-induced compensatory behaviours. In addition, the seemingly modest effect or no effect of exercise on obesity suggests that the role of exercise as a means of weight control needs to be re-appraised and tailored to suit the individual.Current research evidence necessitates determination of the role of individual response to compensatory mechanisms in longer exercise intervention studies under different exercise protocols and varying populations. As metabolic parameters could also constitute a contributing factor to individual differences in compensatory mechanisms (Barwell et al., 2008; King et al., 2007), it is strongly advised that future exercise intervention studies combine investigation of behavioural and metabolic compensatory mechanisms.

In Chapter 3 of this thesis, the impact of acute exercise with EE similar to that recommended for exercise sessions aiming at body weight and body fat reduction (Donnelly et al., 2009; Saris et al., 2003; Jakicic et al., 2001) was investigated on metabolic responses after the consumption of *ad libitum* meals. There are many studies to investigate metabolic impact of exercise in response to fixed meals (Malkova and Gill, 2006). However, this is one of the few recent studies to investigate the effect of exercise on metabolic health variables such as TG, glucose and insulin following *ad libitum* feeding (Farah et al., 2010; King et al., 2010 a,b), which is more reflective of a real life situation. In addition, it is the first study of this kind to be conducted on overweight and obese women. In consistency with Farah et al., (2010), this study demonstrated that a single exercise session can reduce TG response by 17% after *ad libitum* breakfast consumed approximately 14 hours following exercise in overweight and obese individuals. This finding is also in agreement with findings from single exercise studies investigating the impact of exercise on TG responses after a set and usually high-fat meal (Malkova and Gill, 2006). Therefore, this proposes that if repeated on constant basis, exercise sessions with EE close to 2 MJ are likely to diminish postprandial TG concentration, a major risk factor for the development of CVD (Bansal et al., 2007; Nordestgaard et al., 2007; Patsch et al., 2000).

The physical, fitness and metabolic changes exerted in sedentary overweight and obese women by two 8-week supervised cycling exercise programmes, each providing at total 150 minutes of moderate intensity exercise per week and either low frequency/high duration or high frequency/low duration of exercise sessions, were investigated in

Chapter 5. Both programmes, incorporating either 5 x 30 minutes or 2 x 75 minutes of moderate-intensity exercise per week, induced similar changes in fasting insulin concentrations, $HOMA_{IR}$, RMR, predicted $\dot{V}O_2max$, blood pressure, intensity at which LT was achieved and waist circumference in previously sedentary overweight and obese women, with no accompanying changes in body mass and body fat. This study first of all supports previous evidence that exercise can exert physical, fitness and metabolic benefits in the absence of weight loss (Nassis et al., 2009; Church et al., 2007; Nassis et al., 2005; Hasbum et al., 2005; Duncan et al., 2003). In addition, it suggests that varying frequency and duration of exercise sessions does not influence the magnitude of the physical, fitness and metabolic benefits of exercise in overweight and obese women. However, it could be argued that the more frequent sessions are metabolically more beneficial since they induce more frequent 'acute' changes as the chronic effect of both exercise interventions is the same. Given the biomechanical strain of elevated adiposity on human movement (Wearing et al., 2006), it would be expected that overweight and obese women in this study would perceive exercise and especially long duration sessions to be difficult. However, this was not evident with participants being able to complete the 75-minute exercise sessions without any obvious difficulties and excellent overall adherence rates. It is therefore profound, that individuals can be more flexible in planning their physical activity programmes than is currently suggested by physical activity guidelines (Haskell et al., 2007; CMO, 2004) and at the same time this feature provides a viable exercise option for those who struggle to find time to be active on most day of the week.

Among the strengths of the studies presented in this thesis is that the investigated population was constituted of overweight and obese women, a "high-risk" population for the development of chronic disease. Findings definitely give an optimistic edge to the prevention and modulation of risk factors such as obesity, postprandial lipaemia and insulin resistance by means of exercise in this population. It should be noted nevertheless, that these beneficial changes occurred under controlled and supervised conditions. As compliance of participants to the exercise programmes was particularly high, it is evident that supervision by specialists and accountability may be of great assistance to the individuals to achieve specific goals of a programme. However, this fact did not eliminate the possibility of participants compensating for the energy expended outside the exercise programme. It would be therefore important for future research to investigate behavioural response to a supervised regime that includes specific advice and/ or counselling in order to avoid compensatory behaviours outside the exercise programme.

For the measurement of TEE and components in Chapter 4 a method which combines daily HR monitoring with physical activity diaries was used in order to identify compensation factors for the duration of exercise programme (Moon and Butte, 1996). Although, whole body calorimeters are considered as an accurate and reliable technique for the measurement of EE under controlled conditions (Seale et al., 1990), this method is expensive, impractical and cannot be used to measure EE under free-living conditions (Ceesay et al., 1989). The current study required a method that would determine habitual EE in free-living individuals and although DLW is considered one of the most accurate

methods for such a purpose (Levine, 2005; Seale, 1995) it is restrictive in terms of providing only a single measure of TEE. Heart rate monitoring and accelerometry are the two most commonly used methods used to determine free-living patterns of physical activity and EE. Both techniques were considered before deciding on using HR monitoring in the present study. Although accelerometry effectively measures movement, it was opted out because of the substantial limitations in translating accelerometry data into units of EE and the data received cannot easily be calibrated to produce individualised values (Thompson et al., 2006). In contrast, the HR monitoring method utilised in the present study enabled individual calibration of the HR-EE relationship. Problems accosiated with the loss of linearity in the HR-$\dot{V}O_2$ relationship at the low end of the scale were addressed with the approach of Moon and Butte (1996) by sub-dividing activities into 'active' and 'inactive' (and 'sleeping'), based on the activity diary participants filled in concurrently and then using separate functions to determine $\dot{V}O_2$ and EE from HR depending on whether the activity was classed as active or inactive. While not perfect, this combined HR and activity approach has been shown to increase the accuracy of EE estimates beyond assuming a simple linear $\dot{V}O_2$-HR relationship, and shows good agreement with EE measurements made using room calorimetry (Moon and Bute, 1996). The range of prediction errors for 24-h $\dot{V}O2$ and $\dot{V}CO2$ is -3.3 ± 3.5% and -4.6 ± 3% respectively. The intraclass correlation for test-retest reliability of the activity diary used in the this study has been reported as 0.96 for the determination of EE (Bouchard et al., 1983) and this approach is often used as a criterion method for the validation of physical activity questionnaires (Pols et al., 1996). However in this study, this questionnaire was not used to determine energy expenditure, but just to ascertain

whether participants were participating in inactive or active activities at any given time to enable utilisation of the appropriate regression equation to determine EE according to the method of Moon and Butte (1996). This approach has been previously used to calculate EE in obese individuals (Lazzer et al., 2003). Therefore, out of the imperfect methods available the method used in this study seems to be appropriate and at the same time is considered one of the most reliable and accurate methods of EE estimation from HR, in free living conditions (Strath et al., 2000).

In the same study the method to assess diet was based on a 7-day weighed intake as it is deemed by many the "gold standard" technique (Bingham, 1987). According to this, energy intake was found not to be implicated in the process of compensation in nonresponders. However, it is true that as all methods of dietary assessment, it is associated with many limitations such as; relying on the ability and honesty of the individual to record all food and fluid consumed accurately; influencing food choice depending upon the ease at which some foods are measured; altering habitual intake to become more healthy as the individual becomes more aware of the types of food consumed; translating food records into nutritional value by researchers using programmes which may lack up to date food products and can lead to inappropriate substitutions (Johnson, 2002; Hill and Davies, 2001; Schoeller, 1995). The high rate of underreporting in this study in both responders and nonresponders clearly indicates inaccurate recording by a considerable number of participants and therefore the dietary intake data obtained cannot be considered a 100% accurate or reliable reflection of their habitual energy intake. Findings on underreporting are consistent with the findings of

many other studies where the extent of underreporting commonly lies within the range of 20-50% (Hisse et al., 2002) with evidence to suggest the likelihood and extent of underreporting being higher in obese individuals (Schoeller, 1995; Heitmann and Lissner, 1995).

Measurements of the EE and energy intake in intervention studies can be particularly challenging taking into account that human behaviour is very complex. Factors that influence behaviour towards EE and energy intake may vary from physiological to social to hedonic. The burden of excess body weight and the low levels of fitness can act as physical barriers to exercise in obese people. Phychological barriers may include previous negative experiences, lack of confidence, lack of knowledge or experience and shame of being observed (Grilo et al., 1989). Moreover, planned exercise induces fatigue and, thus individuals may be prone to compensate by being inactive for the rest of the day (King et al., 2007). In relation to energy intake, food cues appear to be an important factor influencing both eating and body weight particularly in overweight and individuals concerned with food and weight. The presence of food images, the smell of food or food availability itself could appear to stimulate eating and appetite in humans (Herman and Polivy, 2008). Therefore, a buffet meal, as used in Chapter 3 to measure energy intake may induce food overconsumption. The presence of food may stimulate phychological hunger just as the absence of food causes physiological hunger. As overweight and obese individuals tend to eat less than desired they are likely to be more prone to such hedonic hunger and overeating (Herman and Polivy, 2008). Given that individuals in this study may were in positive energy balance because of confinement in

the lab where not many activities were allowed and overconsuming, estimated food intake may not entirely represent real-life food intake. However, the crossover design of the study should have eliminated any potential differences between the two trials, exercise and rest. In addition the *ad libitum* test meals used to measure energy intake are highly reproducible. The correlation between *ad libitum* energy intake on two separate test days with prior standardization is r= 0.861 (R^2= 0.742, p< 0.0001) (Gregersen et al.,2008).

Limitations associated with the measurement of body fat using bioimpedance scales should also be considered. In comparison to the four component model, considered the "gold standard" method of body composition, the accuracy of Tanita scales is considered poor (Jebb et al., 2000). However, the leg-to-leg bioelectrical impedance method has been shown to have a similar level of accuracy in measuring body fat as alternate methods of bioelectrical impedance as well as the more sophisticated techniques such as underwater weighing in exercise programmes inducing moderate changes in body fat (Minderico et al., 2008; Utter et al., 1999). In Chapters 4 and 5 the predicted changes in body fat mass were considered *a priori* moderate due to the length of the study and the duration of exercise sessions. In the calculations used for the classification of individuals to responders and nonresponders, a change fat mass, without a change in body mass (i.e. a change in fat-free mass) would be detectable as a change in impedance. Although not the gold standard measure, leg-to-leg bioelectrical impedance can detect changes in body composition with in response to diet and/or exercise interventions (Minderico et al., 2008; Utter et al., 1999) and has good test-retest reliability but huge variance. Waist

circumference measurements as opposed to bioimpedance measurements are reported to be highly reproducible (Berker et al., 2010). However, in populations with BMI > 25 the correlation between waist circumference measurements and fat mass is decreased, which is thought to reflect problems in measuring overweight and obese individuals due to increased fat mass and between-examiner and within-examiner variation (Berker et al., 2010; van de Kooy and Seidell, 1993; Busetto et al., 1992).

A limitation in the acute study presented in Chapter 3 is that plasma hormones supposed to be related with appetite regulation were not measured, unlikely other studies of the same nature (Martins et al., 2008). There are few studies to show altered appetite and hormonal responses following acute exercise, however, it should be noted that findings are quite inconsistent and rarely there is a concordance between the seemingly related measures (Hagobian and Braun, 2010; Martins et al., 2008). This disconnection probably stems from the fact that energy regulating hormones and appetite respond to different physiological and metabolic signals (Borer et al., 2009). In Chapter 3, no measurement of hormonal responses limits the mechanistic interpretation of the data obtained, nevertheless it could be inferred that these measurements would add no additional value to the measurements of energy intake, which on its own allows understanding of compensatory changes in energy balance.

Finally, another limitation relates to the duration of the exercise training programme as well as the post-intervention observation period following a single exercise session. It is likely that the responses observed under these circumstances may differ to the effects observed if the trials were continued for longer, as would in a “real-life” situation. It is

therefore proposed, that future research considers first of all the implementation of longer observatory periods after acute exercise, considering the hypothesis that a critical point exists when energy intake increases to match EE (Melzer et al., 2005; Blundell et al., 2003; Blundell and King, 1999). Secondly, there is a need for longer exercise intervention studies to investigate the role of individual response to compensatory mechanisms. In addition, it would be very interesting to find out whether nonresponders could be identified after an acute exercise session and subsequently targeted with healthy behavioural advice and/ or counselling on the top of a long term exercise regime. Finally, this thesis was limited to the investigation of overweight and obese women. For this reason, it is judged critical that energy balance and metabolic changes derived from exercise employment should be investigated in other high-risk populations such as overweight and obese men or severely obese individuals.

Conclusions

Overweight and obese women do not compensate in terms of appetite and energy intake for the energy expended in a single exercise session similar to that recommended for individual exercise sessions aiming at body weight and body fat loss. This finding gives exercise credentials as a meaningful tool in weight management planning.

Compensatory responses in terms of changes in energy intake are also not evident in overweight and obese women participating in an 8-week exercise training programme. However, predicted body fat loss can be achieved only in those who during exercise programme do not decrease physical activity outside exercise sessions. By recognising

that some overweight and obese women partaking in exercise programmes compensate by being less active outside exercise sessions, health professionals should design individually tailored training programmes which include appropriate counseling and/or advice in order to increase the likelihood of successful body fat loss. By acknowledging the response to exercise as individual, exercise can be considered a useful tool for weight management in the prevention and treatment of obesity.

A single exercise session with EE similar to that recommended for individual exercise sessions aiming at body mass and body fat loss, favourably modifies responses of TG to *at libitum* breakfast consumed approximately 14 hours following an exercise session. Clinical implications of this finding, suggest that exercise may be of particular help to individuals predisposed to metabolic risk factors for the development of CVD.

Changes in fitness, insulin resistance, diastolic blood pressure and waist circumference in sedentary overweight and obese women induced by an 8-week exercise programme incorporating 150 minutes of exercise per week are independent of frequency and duration of exercise sessions with 2 x 75 minute exercise sessions per week and 5 x 30 minute exercise sessions per week eliciting similar changes. This finding makes an important contribution to current physical activity for health guidelines suggesting that individuals can be flexible in their pattern of exercise throughout the week, provided the total weekly volume of exercise undertaken remains as recommended. This may be attractive for individuals who find it difficult to undertake physical activity on most days of the week.

REFERENCES

Almeras, N., Lavallee, N., Despres, J.P., Bouchard, C., Tremblay, A. (1999). Exercise and energy intake: effect of substrate oxidation. *Physiology and Behaviour,* **57**, 995-1000.

Altena, T.S., Michaelson, J.L., Ball, S.D., Thomas, T.R. (2004). Single sessions of intermittent and continuous exercise and postprandial lipemia. *Medicine and Science in Sports and Exercise*, **36(8)**, 1364-1371.

American College of Sports Medicine. (1975). Guidelines for graded exercise testing and exercise prescription. Philadelphia: Lea & Febiger.

American College of Sports Medicine. (1978). Position statement on the recommended quantity and quality of exercise for developing and maintaining fitness in healthy adults. *Medicine and Science in Sports and Exercise,* **10**, vii-x.

American College of Sports Medicine. (1980). Guidelines for graded exercise testing and exercise prescription. Philadelphia: Lea & Febiger, 1980.

American College of Sports Medicine. (1986). Guidelines for exercise testing and prescription. Philadelphia: Lea & Febiger.

American College of Sports Medicine. (1991). Guidelines for exercise testing and prescription. Malvern, PA: Lea & Febiger.

American College of Sports Medicine. (1995). ACSM's guidelines for exercise testing and prescription. Media, PA: Williams & Wilkins.

American College of Sports Medicine Position Stand. (1998).The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Medicine and Science in Sports and Exercise*, **30**, 975–991.

Andersson, B., Xu, X.F., Rebuffé-Scrive, M., Terning, K., Krotkiewski, M., Björntorp, P. (1991). The effects of exercise, training on body composition and metabolism in men and women. *International Journal of Obesity*, **15(1)**, 75-81.

A report from the Chief Medical Officer. (2004). At least five a week: Evidence on the impact of physical activity and its relationship to health. UK: Department of Health.

Austin, M.A., King, M.C., Vranizan, K.M., Krauss, R.M. (1990). Atherogenic lipoprotein phenotype. A proposed genetic marker for coronary heart disease risk. *Circulation*, **82**, 495-506.

Azevedo, J.L., Carey, J.O., Pories, W.J., Morris, P.G., Dohm, G.L. (1995). Hypoxia stimulates glucose transport in insulin-resistant human skeletal muscle. *Diabetes*, **44**, 695-698.

Bae, J.H., Bassenge, E., Kim, K.B., Kim, Y.N., Kim, K.S., Lee, H.J., Moon, K.C., Lee, M.S., Park, K.Y., Schwemmer, M. (2001). Postprandial hypertriglyceridemia impairs endothelial function by enhanced oxidant stress. *Atherosclerosis*, **155**, 517-523.

Ballor, D.L., Keesey, R.E. (1991). A meta-analysis of the factors affecting exercise-induced changes in body mass, fat mass and fat-free mass in males and females. *International Journal of Obesity*, **15(11)**, 717-726.

Bansal, S., Buring, J.E., Rifai, N., Mora, S., Sacks, F.M., Ridker, P.M. (2007). Fasting compared with nonfasting triglycerides and risk of cardiovascular events in women. *JAMA*, **298(3)**, 309-316.

Barlow, C.E., LaMonte, M.J., Fitzgerald, S.J., Kampert, J.B., Perrin, J.L., Blair, S.N. (2006). Cardiorespiratory fitness is an independent predictor of hypertension incidence among initially normotensive healthy women. *American Journal of Epidemiology*, **163(2)**, 142-150.

Barnes, P. (2007). Physical activity among adults: United States, 2000 and 2005. Hyattsville, MD: US Department of Health and Human Services, CDC.

Barwell, N.D., Malkova, D., Moran, C.N., Cleland, S.J., Packard, C.J., Zammit, V.A., Gill, J.M. (2008). Exercise training has greater effects on insulin sensitivity in daughters of patients with type 2 diabetes than in women with no family history of diabetes. *Diabetologia*, **51(10)**, 1912-1919.

Bauman, A., Bull, F., Chey, T., Craig, C.L., Ainsworth, B.E., Sallis, J.F., Bowles, H.R., Hagstromer, M., Sjostrom, M., Pratt, M., The IPS Group. (2009). The International Prevalence Study on Physical Activity: results from 20 countries. *International Journal of Behavioral Nutrition and Physical Activity*, **6**, 21.

Beavers, K.M., Hsu, F.C., Isom, S., Kritchevsky, S.B., Church, T., Goodpaster, B., Pahor, M., Nicklas, B.J. (2010). Long-Term Physical Activity and Inflammatory Biomarkers in Older Adults. *Medicine and Science in Sports and Exercise*. **in print**

Benjamin, M., Hillen, B. (2003). Mechanical influences on cells, tissues and organs - 'Mechanical Morphogenesis'. *European Journal of Morphology*, **41(1)**, 3-7.

Berg, A.H., Scherer, P.E. (2005). Adipose tissue, inflammation, and cardiovascular disease. *Circulation Research*, **96**, 939-949.

Berghöfer, A., Pischon, T., Reinhold, T., Apovian, C.M., Sharma, A.M., Willich, S.N. (2008). Obesity prevalence from a European perspective: a systematic review. *BMC Public Health*, **8**, 200.

Berker, D., Koparal, S., Işik, S., Paşaoğlu, L., Aydin, Y., Erol, K., Delibaşi, T., Güler ,S. (2010). Compatibility of different methods for the measurement of visceral fat in different body mass index strata. *Diagnostic and Intervational Radiology.* **16(2)**, 99-105.

Bilski, J., Teległów, A., Zahradnik-Bilska, J., Dembiński, A., Warzecha, Z. (2009). Effects of exercise on appetite and food intake regulation. *Medicina Sportiva*, **13(2)**, 82-94.

Bingham, S. A. (1987). The dietary assessment of individuals; methods, accuracy, new techniques and recommendations. *Nutrition Abstract Reviews,* **57**, 705 – 742.

Black, A.E., Cole, T.J. (2001). Biased over- or under-reporting is characteristic of individuals whether over time or by different assessment methods. *Journal of American Dietetic Association,* **101**, 70–80.

Bluher, M., Unger, R., Rassoul, F., Richter, V., Paschke, R. (2002). Relation between glycaemic control, hyperinsulinaemia and plasma concentrations of soluble adhesion molecules in patients with impaired glucose tolerance or type II diabetes. *Diabetologia*, **45**, 210 –216.

Blair, S. N., Kampert, J. B., Kohl, III, H. W. et al. (1996). Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. *JAMA*, **276**, 205–210.

Blair, S. N., Cheng, Y., Holder, J. S. (2001). Is physical activity or physical fitness more important in defining health benefits? *Medicine and Science in Sports and Exercise*, **33**, S379–S399.

Blair, S.N., Church, T.S. (2004). The fitness, obesity, and health equation: is physical activity the common denominator? *JAMA*, **292(10)**, 1232-1234.

Bleich, S., Cutler, D., Murray, C., Adams, A. (2008). Why is the developed world obese? *Annual Reviews of Public Health*, **29**, 273-295.

Blundell, J.E., King, N.A. (1999). Physical activity and regulation of food intake: current evidence. *Medicine and Science in Sports and Exercise*, **31(11)**, S573–S583.

Blundell, J.E., Stubbs, R.J., Hughes, D.A., Whybrow, S., King, N.A. (2003). Cross talk between physical activity and appetite control: does physical activity stimulate appetite? *Proceedings of Nutrition Society*, **62(3)**, 651-661.

Blundell, J.E., Stubbs, R.J., Golding, C., Croden, F., Alam, R., Whybrow, S., Le Noury, J., Lawton, C.L. (2005). Resistance and susceptibility to weight gain: individual variability in response to a high-fat diet. *Physiology and Behaviour*, **86(5)**, 614-622.

Bo, S., Pisu, E. (2008). Role of dietary magnesium in cardiovascular disease prevention, insulin sensitivity and diabetes. *Current Opinion in Lipidology*, **19(1)**, 50-56.

Boden, G., Shulman, G. I. (2002). Free fatty acids in obesity and type 2 diabetes: defining their role in the development of insulin resistance and beta-cell dysfunction. *European Journal of Clinical Investigation*, **32(3)**, 14-23.

Bond, V., Stephens, Q., Adams, R.G., Vaccaro, P., Demeersman, R., Williams, D., Obisesan, T.O., Franks, B.D., Oke, L.M., Coleman, B., Blakely, R., Millis, R.M. (2002). Aerobic exercise attenuates an exaggerated exercise blood pressure response in normotensive young adult African-American men. *Blood Pressure*, **11(4)**, 229-234.

Bordenave, S., Brandou, F., Manetta, J., Fédou, C., Mercier, J., Brun, J.F. (2008). Effects of acute exercise on insulin sensitivity, glucose effectiveness and disposition index in type 2 diabetic patients. *Diabetes and Metabolism*, **34(3)**, 250-257.

Borer, K.T., Wuorinen, E., Ku, K., Burant, C. (2009). Appetite responds to changes in meal content, whereas ghrelin, leptin, and insulin track changes in energy availability. *Journal of Clinical Endocrinology and Metabolism*, **94(7)**, 2290-2298.

Borg, G.A. (1974). Perceived exertion. *Exercise and Sport Sciences Reviews*, **2**, 131-153.

Borghouts, L. B., Keizer, H. A. (2000). Exercise and insulin sensitivity: a review. *International Journal of Sports Medicine*, **21(1)**, 1-12.

Bouchard, C., Tremblay, A., Leblanc, C., Lortie, G., Savard, R., Theriault, G. (1983). A method to assess energy expenditure in children and adults. *American Journal of Clinical Nutrition*, **37**, 461–467.

Bouchard, C., Tremblay, A., Nadeau, A., et al. (1990). Long-term exercise training with constant energy intake. 1: effect on body composition and selected metabolic variables. *International Journal of Obesity*, **14**, 57–73.

Boutcher, S.H., Dunn, S.L. (2009). Factors that may impede the weight loss response to exercise-based interventions. *Obesity Reviews*, **10(6)**, 671-680.

Broeder, C.E., Burrhus, K.A., Svanevik, L.S., Wilmore, J.H. (1992). The effects of either high-intensity resistance or endurance training on resting metabolic rate. *American Journal of Clinical Nutrition*, **55**, 802-810.

Broom, D.R., Batterham, R.L., King, J.A., Stensel, D.J. (2009). Influence of resistance and aerobic exercise on hunger, circulating levels of acylated ghrelin , and peptide YY in healthy males. *American Journal of Physiology- Regulatory Integrative Comparative Physiology*, **296(1)**, R29-35.

Brozinick, J.T. Jr, Etgen, G.J., Yaspelkis, B.B. III, Ivy, J.L. (1992). Contraction-activated glucose uptake is normal in insulin-resistant muscle of the obese Zucker rat. *Journal of Applied Physiology*, **73**, 382-387.

Brozinick, J.T. Jr, Etgen, G.J., Yaspelkis, B.B. III, Ivy, J.L. (1994). Glucose uptake and GLUT-4 protein distribution in skeletal muscle of obese Zucker rat. *American Journal of Physiology- Regulatory Integrative Comparative Physiology*, **267**, R236-R243.

Bruce, C.R., Anderson, M.J., Carey, A.L., Newman, D.G., Bonen, A., Kriketos, A.D., Cooney, G.J., Hawley, J.A. (2003). Muscle oxidative capacity is a better predictor of insulin sensitivity than lipid status. *Journal of Clinical Endocrinology and Metabolism*, **88**, 5444-5451.

Bruce, C.R., Thrush, A.B., Mertz, V.A., Bezaire, V., Chabowski, A., Heigenhauser, G.J., Dyck, D.J. (2006). Endurance training in obese humans improves glucose tolerance and mitochondrial fatty acid oxidation and alters muscle lipid content. *American Journal of Physiology Endocrinology and Metabolism*, **291(1)**, E99-E107.

Busetto, L., Baggio, M.B., Zurlo, F., Carraro, R., Digito, M., Enzi, G. (1992). Assessment of abdominal fat distribution in obese patients: anthropometry versus computerized tomography. *International Journal of Obesity and Related Metabolic Disorders*. **16(10)**, 731-736.

Caspersen, C.J., Powell, K.E., Christenson, G.M. (1985). Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Reports,* **100**, 126–131.

Cecil, J.E., Tavendale, R., Watt, P., Hetherington, M.M., Palmer, C.N. (2008). An obesity-associated FTO gene variant and increased energy intake in children. *New England Journal of Medicine*, **359(24)**, 2558-2566.

Centers for Disease Control and Prevention (CDC). (2008). Prevalence of Regular Physical Activity Among Adults- United States, 2001 and 2005. *JAMA*, **299(1)**, 30-32.

Ceesay, S.M., Prentice, AM., day, K.C. et al. (1989). The use of heart rate monitoring in the estimation of energy expenditure: a validation study using indirect whole body calorimetry. *British journal of Nutrition*, **61,** 175-186.

Chief Medical Officer (CMO). (2004). At Least Five a Week: Evidence on the impact of physical activity and its relationship to health. London: Department of Health.

Christ- Roberts, C.Y., Mandarino, L.J. (2004). Glycogen synthase: key effect of exercise on insulin action. *Exercise and Sport Sciences Reviews*, **32**, 90-94.

Church, T.S., Earnest, C.P., Skinner, J.S., Blair, S.N. (2007). Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: a randomized controlled trial. *JAMA*, **297(19)**, 2081-2091.

Church, T.S., Martin, C.K., Thompson, A.M., Earnest, C.P., Mikus, C.R., Blair, S.N. (2009). Changes in weight, waist circumference and compensatory responses with different doses of exercise among sedentary, overweight postmenopausal women. *Plos One*. **4**, e4515.

Cines, D.B., Pollak, E.S., Buck, C.A., Loscalzo, J., Zimmerman, G.A., McEver, R.P., Pober, J.S., Wick, T.M., Konkle, B.A., Schwartz, B.S., et al., (1998). Endothelial cells in physiology and in the pathophysiology of vascular disorders. *Blood*, **91(10)**, 3527-3561.

Clarkson, P., Montgomery, H. E., Mullen, M. J., Donald, A.E., Powe, A.J., Bull, T., Jubb, M., World, M., Deanfield, J.E. (1999). Exercise training enhances endothelial function in young men. *Journal of American College Cardiology*, **33**, 1379–1385.

Coakley, E.H., Kawachi, I., Manson, J.E., Speizer, F.E., Willet, W.C., Colditz, G.A. (1998). Lower levels of physical functioning are associated with higher body weight

among middle-aged and older women. *International Journal of Obesity and Related Metabolic Disorders*, **22(10)**, 958-965.

Cohn, J.S. (1998). Postprandial lipemia: emerging evidence for atherogenicity of remnant lipoproteins. *Canadian Journal of Cardiology*. **14(B)**, 18B-27B.

Colberg, S.R., Grieco, C.R. (2009). Exercise in the treatment and prevention of diabetes. *Current Sports Medicine Reports*, **8(4)**, 169-175.

Colley, R.C., Hills, A.P., O'Moore-Sullivan, T.M., Hickman, I.J., Prins, J.B., Byrne, N.M. (2008). Variability in adherence to an unsupervised exercise prescription in obese women. *International Journal of Obesity*, **32**, 837-844.

Cox, K.L., Burke, V., Morton, A.R., Beilin, L.J., Puddey, I.B. (2003). The independent and combined effects of 16 weeks of vigorous exercise and energy restriction on body mass and composition in free-living overweight men – a randomised controlled trial. *Metabolism*, **52**, 107-115.

Craig, C., Russell, S., Cameron, C., Bauman, A. (2004). Twenty-year trends in physical activity among Canadian adults. *Canadian Journal of Public Health*, **95(1)**, 59-63.

Dallongeville, J., Martínez-Gómez, D., Bokor, S., Manios, Y., et al., (2010). for the HELENA study group attenuation of the effect of the FTO rs9939609 polymorphism on

total and central body fat by physical activity in adolescents. *Archives in Pediatric and Adolescent Medicine*, **164(4)**, 328-333.

Dattilo, A.M., Kris-Etherton, P.M. (1992). Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. *American Journal of Clinical Nutrition*, **56**, 320–328.

Davies, M.J., Gordon, J.L., Gearing, A.J., Pigott, R., Woolf, N., Katz, D., Kyriakopoulos, A. (1993). The expression of the adhesion molecules ICAM-1, VCAM-1, PECAM, and E-selectin in human atherosclerosis. *Journal of Pathology*, **171(3)**, 223-229.

DeBusk, R.F., Stenestrand, U., Sheehan, M., Haskell, W.L. (1990). Training effects of long versus short bouts of exercise in healthy subjects. *American Journal of Cardiology*, **65**, 1010-1013.

Delarue, J., Magnan, C. (2007a). Free fatty acids and insulin resistance. *Current Opinion in Clinical Nutrition and Metabolic Care*, **10(2)**, 142-148.

Dengel, D.R., Pratley, R.E., Hagberg, J.M., Rogus, E.M., Goldberg, A.P. (1996). Distinct effects of aerobic exercise training and weight loss on glucose homeostasis in obese sedentary men. *Journal of Applied Physiology*, **81(1)**, 318-325.

Department for Environment Food and Rural Affairs. (2007). UK purchases and expenditure on food and drink and derived energy and nutrient intakes in 2005-2006. UK: National Statistics.

Despres, J.P., Lemieux, I., Prud'homme, D. (2001). Treatment of obesity: need to focus on high risk abdominally obese patients. *British Medical Journal*, **322**, 716–720.

Després, J.P., Lemieux, I. (2006). Abdominal obesity and metabolic syndrome. *Nature*, **444(7121)**, 881-887.

DiPietro, L., Dziura, J., Yeckel, C.W., Neufer, P.D. (2006). Exercise and improved insulin sensitivity in older women: evidence of the enduring benefits of higher intensity training. *Journal of Applied Physiology*, **100(1)**, 142-149.

Ditschuneit, H.H., Flechtner-Mors, M., Johnson, T.D., Adler, G. (1999). Metabolic and weight-loss effects of a long-term dietary intervention in obese patients. *American Journal of Clinical Nutrition*, **69,** 198–204.

Doi, H., Kugiyama, K., Ohgushi, M., Sugiyama, S., Matsumura, T., Ohta, Y., Nakano, T., Nakajima, K., Yasue, H. (1998). Remnants of chylomicron and very low density lipoprotein impair endothelium-dependent vasorelaxation. *Atherosclerosis*, **137**, 341-349.

Donnelly, J.E., Jacobsen, D.J., Heelan, K.S., Seip, R., Smith, S. (2000). The effects of 18 months of intermittent vs. continuous exercise on aerobic capacity, body weight and composition, and metabolic fitness in previously sedentary, moderately obese females. *International Journal of Obesity and Related Metabolic Disorders*, **24(5)**, 566-572.

Donnelly, J.E., Kirk, E.P., Jacobsen, D.J., Hill, J.O., Sullivan, D.K., Johnson, S.L. (2003). Effects of 16 months of verified, supervised aerobic exercise on macronutrient intake in overweight men and women: the Midwest exercise trial. *American Journal of Clinical Nutrition*, **78**, 950-956.

Donnelly, J.E., Smith, B.K. (2005). Is exercise effective for weight loss with *ad libitum* diet? Energy balance, compensation, and gender differences. *Exercise and Sport Sciences Reviews*, **33**, 169–174.

Donnelly, J.E., Blair, S.N., Jakicic, J.M., Manore, M.M., Rankin, J.W., Smith, B.K; American College of Sports Medicine. (2009). American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. *Medicine and Science in Sports and Exercise*, **41(2)**, 459-471.

Douketis, J.D., Macie, C., Thabane, L., Williamson, D.F. (2005). Systematic review of long-term weight loss studies in obese adults: clinical significance and applicability to clinical practice. *International Journal of Obesity*, **29(10)**, 1153-1167.

Duncan, B.B., Schmidt, M.I., Pankow, J.S., Ballantyne, C.M., Couper, D., Vigo, A., Hoogeveen, R., Folsom, A.R., Heiss, G. (2003). Low-grade systemic inflammation and the development of type 2 diabetes: the atherosclerosis risk in communities study. *Diabetes,* **52**, 1799–1805.

Duncan, G.E., Perri, M.G., Theriaque, D.W., Hutson, A.D., Eckel, R.H., Stacpoole, P.W. (2003). Exercise training, without weight loss, increases insulin sensitivity and postheparin plasma lipase activity in previously sedentary adults. *Diabetes Care*, **26(3)**, 557-562.

Duncan, G.E. (2010). The "fit but fat" concept revisited: population-based estimates using NHANES. *International Journal of Behavioural Nutrition and Physical Activity,* **7(1)**, 47.

Duncan, J.J., Gordon, N.F., Scott, C.B. (1991). Women walking for health and fitness. How much is enough? *JAMA*, **266(23)**, 3295-3299.

Dunn, A.L., Marcus, B.H., Kampert, J.B., Garcia, M.E., Kohl, H.W. 3rd, Blair, S.N. (1999). Comparison of lifestyle and structured interventions to increase physical activity and cardiorespiratory fitness: a randomized trial. *JAMA*, **281(4)**, 327-334.

Eaton, S.B., Shostak, M., Konner, M. (1988). *Paleolithic Prescription*, pp 168. New York: Harper and Row.

Ebisu, T. (1985). Splitting the distance of endurance running: on cardiovascular endurance and blood lipids. *Jpn Journal of Physical Education*, **30**, 37-43.

Elia, M., Stratton, R., Stubbs, J. (2003). Techniques for the study of energy balance in man. *Proceedings of Nutrition Society*, **62**, 529-537.

Elder, S.J., Roberts, S.B. (2007). The effects of exercise on food intake and body fatness: A summary of published studies. *Nutrition Reviews*, **65**, 1-19.

Epstein, L.H. Wing, R.R. (1980). Aerobic exercise and weight. *Addictive Behaviours*, **5**, 371-338.

Erdmann, J., Tahbaz, R., Lippl, F., Wagenpfeil, S., Schusdziarra, V. (2007). Plasma ghrelin levels during exercise - effects of intensity and duration. *Regulatory Peptides*, **143(1-3)**, 127-35.

Eriksen, L., Dahl-Petersen, I., Haugaard, S.B., Dela, F. (2007). Comparison of the effect of multiple short-duration with single long-duration exercise sessions on glucose homeostasis in type 2 diabetes mellitus. *Diabetologia*, **50(11)**, 2245-2253.

Eriksson, J., Tuominen, J., Valle, T., Sundberg, S., Sovijari, A., Lindholm, H., Tuomilehto, J., Koivisto, V. (1998). Aerobic endurance exercise or circuit-type resistance training for individuals with impaired glucose tolerance? *Hormonal and Metabolic Research*, **30**, 37-41.

Eriksson, J., Lindström, J., Valle, T., Aunola, S., Hämäläinen, H., Ilanne-Parikka, P., Keinänen-Kiukaanniemi, S., Laakso, M., Lauhkonen, M., Lehto, P., et al., (1999). Prevention of Type II diabetes in subjects with impaired glucose tolerance: the Diabetes Prevention Study (DPS) in Finland. Study design and 1-year interim report on the feasibility of the lifestyle intervention programme. *Diabetologia*, **42(7)**, 793-801.

Erlichman, J., Kerbey, A.L., James, W.P. (2002). Physical activity and its impact on health outcomes. Paper 2: Prevention of unhealthy weight gain and obesity by physical activity: an analysis of the evidence. *Obesity Reviews*, **3(4)**, 273-287.

Ershow, A.G., Hill, J.O., Baldwin, J.T. (2004). Novel engineering approaches to obesity, overweight, and energy balance: public health needs and research opportunities. *Proceedings of the 26th Annual International Conference of the IEEE EMBS*, 5212-5214.

Essig, D.A., Alderson, N.L., Ferguson, M.A., Bartoli, W.P., Durstine, J.L. (2000). Delayed effects of exercise on the plasma leptin concentration. *Metabolism*, **49(3)**, 395-399.

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. (2001). Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *JAMA*, **285**, 2486–97.

Fallon, K.E., Fallon, S.K., Boston, T. (2001). The acute phase response and exercise: court and field sports. *British Journal of Sports Medicine*, **35**, 170–173.

Farah, N.M., Malkova, D., Gill, J.M. (2010). Effects of exercise on postprandial responses to ad libitum feeding in overweight men. *Medicine and Science in Sports and Exercise*, **in press**

Febbraio, M.A., Pedersen, B.K. (2002). Muscle-derived interleukin-6: mechanisms for activation and possible biological roles. *FASEB Journal*, **16**, 1335–1347.

Ferguson, M.A., Alderson, N.L., Trost, S.G., Essig, D.A., Burke, J.R., Durstine, J.L. (1998). Effects of four different single exercise sessions on lipids, lipoproteins, and lipoprotein lipase. *Journal of Applied Physiology*, **85(3)**, 1169-1174.

Festa, A., D'Agostino, R. Jr., Tracy, R.P., Haffner, S.M. (2002). Elevated levels of acute-phase proteins and plasminogen activator inhibitor-1 predict the development of type 2 diabetes: the insulin resistance atherosclerosis study. *Diabetes*, **51**, 1131–1137.

Finlayson, G., Bryant, E., Blundell, J.E., King, N.A. (2009). Acute compensatory eating following exercise is associated with implicit hedonic wanting for food. *Physiology and Behaviour*, **97(1)**, 62-67.

Flechtner-Mors, M., Ditschuneit, H.H., Johnson, T.D., Suchard, M.A., Adler, G. (2000). Metabolic and weight loss effects of long-term dietary intervention in obese patients: four-year results. *Obesity Research*, **8,** 399–402.

Flegal, K.M. Graubard, B.I., Williamson, D.F., et al., (2005). Excess deaths associated with underweight, overweight, and obesity. *JAMA*, **293(15)**, 1861-1867.

Flegal, K.M., Carroll, M.D., Ogden, C.L., Curtin, L.R. (2010). Prevalence and trends in obesity among US adults, 1999-2008. *JAMA*, **303(3)**, 235-241.

Fletcher, G.F., Blair, S.N., Blumenthal, J., Caspersen, C., Chaitman, B., Epstein, S., Falls, H., Froelicher, E.S., Froelicher, V.F., Pina, I.L. (1992). Statement on exercise. Benefits and recommendations for physical activity programs for all Americans. A statement for health professionals by the Committee on Exercise and Cardiac

Rehabilitation of the Council on Clinical Cardiology, American Heart association. *Circulation*, **86(1)**, 340-344.

Flint, A., Raben, A., Blundell, J.E., Astrup, A. (2000). Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies. *International Journal of Obesity*, **24**, 28-48.

Fogelholm, M., Kukkonen-Harluja, K. (2000). Does physical activity prevent weight gain-a systematic review. *Obesity Reviews*, **1(2)**, 95-111.

Folsom, A.R., Kushi, L.H., Hong, C.P. (2000). Physical activity and incident diabetes mellitus in postmenopausal women. *American Journal of Public Health*, **90(1)**, 134-138.

Ford, E.S., Mokdad, A.H. (2008). Epidemiology of obesity in the Western Hemisphere. *Journal of Clinical Endocrinology and Metabolism*. **93(11)**, S1-8.

Fox, K.R., Hillsdon, M. (2007). Physical activity and obesity. *Obesity Reviews*, **8(1)**, 115-121.

Franz, M.J., VanWormer, J.J., Crain, A.L., Boucher, J.L., Histon, T., Caplan, W., et al., (2007). Weightloss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *Journal of American Dietetic Association*, **107**, 1755-1767.

Frayling, T.M., Timpson, N.J., Weedon, M.N., Zeggini, E., Freathy, R.M., Lindgren, C.M., Perry, J.R., Elliott, K.S., Lango, H., Rayner, N.W., et al., (2007). A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. *Science*, **316(5826)**, 889-894.

Frayn, K.N., Macdonald, I.A. (1997). Assessment of substrate and energy metabolism in vivo. In: Draznin B, Rizza R (eds). Clinical Research in Diabetes and Obesity Part I: Methods, Assessment, and Metabolic Regulation, pp 101-124. Totowa NJ: Humana Press.

Freeman, D.J., Norrie, J., Caslake, M.J., Gaw, A., Ford, I., Lowe, G.D., O'Reilly, D.S., Packard, C.J., Sattar, N. (2002). C-reactive protein is an independent predictor of risk for the development of diabetes in the West of Scotland Coronary Prevention Study. *Diabetes*, **51**, 1596–1600.

Friedewald, W.T., Levy, R.I., Fredrickson, D.S. (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical Chemistry*, **18**, 499–502.

Ford, E.S. (2002). Leukocyte count, erythrocyte sedimentation rate, and diabetes incidence in a national sample of US adults. *American Journal of Epidemiology*, **155**, 57–64.

Funada, J., Sekiya, M., Hamada, M., Hiwada, K. (2002). Postprandial elevation of remnant lipoprotein leads to endothelial dysfunction. *Circulation Journal*, **66**, 127-132.

Garrow, J.S., Summerbell, C.D. (1994). Meta-analysis: effect of exercise, with or without dieting, on body composition of overweight subjects. *European Journal of Clinical Nutrition,* **49**.

Geffken, D.F., Cushman, M., Burke, G.L., Polak, J.F., Sakkinen, P.A., Tracy, R.P. (2001). Association between physical activity and markers of inflammation in a healthy elderly population. *American Journal of Epidemiology*, **153**, 242–250.

George, V.A., Morganstein, A. (2003). Effect of moderate intensity exercise on acute energy intake in normal and overweight females. *Appetite*, **40**, 43-46.

Gill, J., Murphy, M.H., Hardman, A.E. (1998). Postprandial lipemia: effects of intermittent versus continuous exercise. *Medicine and Science in Sports and Exercise,* **30(10)**, 1515-1520.

Gill, J.M.R., Caslake, M.J., McCallister, C. **et al.** Effects of short-term detraining on postprandial metabolism, endothelial function, and inflammation in endurance-trained men: dissociation between changes in triglyceride metabolism and endothelial function. *Journal of Clinical Endocrinology and Metabolism*, **88(9)**, 4328-4335.

Gill, J.M., Hardman, A.E. (2003). Exercise and postprandial lipid metabolism: an update on potential mechanisms and interactions with high- carbohydrate diets (review). *Journal of Nutritional Biochemistry*, **14**, 122-132.

Gill, J.M.R. (2004). Exercise and postprandial lipid metabolism- an analysis of the current evidence. *European Journal of Lipid Science and Technology*, **106**, 110-121.

Gill, J.M., Malkova, D. (2006). Physical activity, fitness and cardiovascular disease risk in adults: interactions with insulin resistance and obesity. Clinical Science, **110(4)**, 409-425.

Goldberg, G.R., Prentice, A.M., Davies, H.L., Murgatroyd, P.R. (1988). Overnight and basal metabolic rates in men and women. *European Journal of Clinical Nutrition*, **42**, 137–144.

Goodfriend, T.L., Kelley, D.E., Goodpaster, B.H., Winters, S.J. (1999). Visceral obesity and insulin resistance are associated with plasma aldosterone levels in women. *Obesity Research*, **7(4)**, 355-362.

Goran, M.I., Poehlman, E.T. (1992). Endurance training does not enhance total energy expenditure in healthy elderly persons. *American Journal of Physiology*, **263**, E950-957.

Goris, A.H., Westerterp-Plantenga, M.S., Westerterp, K.R. (2000). Undereating and underrecording of habitual food intake in obese men: selective underreporting of fat intake. *American Journal of Clinical Nutrition*, **71(1)**, 130-134.

Green, D. J., Cable, N. T., Fox, C., Rankin, J. M. and Taylor, R. R. (1994) Modification of forearm resistance vessels by exercise training in young men. *Journal of Applied Physiology*, **77**, 1829–1833.

Gregersen, N.T., Flint, A., Bitz, C., Blundell, J.E., Raben, A., Astrup, A. (2008) Reproducibility and power of ad libitum energy intake assessed by repeated single meals. *American Journal of Clinical Nutrition*, **87(5)**, 1277-1281.

Griffin, B.A. (1997). Low-density lipoprotein subclasses: mechanisms of formation and modulation. *Proceedings of Nutrition Society*, **56(2)**, 693-702.

Grilo, C.M., Shiffman, S., Wing, R.R. Relapse crises and coping among dieters. (1989). *Journal of Consultation and Clinical Psychology*, **57(4)**, 488-495.

Grundy, S.M. (2004). Obesity, metabolic syndrome, and cardiovascular disease. *Journal of Clinical Endocrinology and Metabolism*, **89(6)**, 2595-2600.

Haag, M., Dippenaar, N.G. (2005). Dietary fats, fatty acids and insulin resistance: short review of a multifaceted connection. *Medical Science Monitor*, **11(12)**, RA359-367.

Haapanen, N., Miilunpalo, S., Pasanen, M., Oja, P., Vuori, I. (1997). Association between leisure time physical activity and 10-year body mass change among working-aged men and women. *International Journal of Obesity and Related Metabolic Disorders*, **21(4)**, 288-296.

Hagobian, T.A., Brau, B. (2010). Physical activity and hormonal regulation of appetite: sex differences and weight control. *Exercise and Sport Science Reviews*, **38(1)**, 25-30.

Hambrecht, R., Fiehn, E., Weigl, C., et al., (1998). Regular physical exercise corrects endothelial dysfunction and improves exercise capacity in patients with chronic heart failure. *Circulation*, **98**, 2709-2715.

Hammett, C.J., Prapavessis, H., Baldi, J.C., (2006) **et al.** Effects of exercise training on 5 inflammatory markers associated with cardiovascular risk. *American Heart Journal*. **151**, 367.

Hansen, A.K., Fischer, C.P., Plomgaard, P., Andersen, J.L., Saltin, B., Pedersen, B.K. (2005). Skeletal muscle adaptation: training twice every second day vs. training once daily. *Journal of Applied Physiology*, **98(1)**, 93-99.

Hardman, A.E., Lawrence, J.E.M., Herd, S.L. (1998). Postprandial lipemia in endurance-trained people during a short interuption to training. *Journal of Applied Physiology*, **84(6)**, 1895-1901.

Harrison, M., Nertney, L., O'Gorman, D., Moyna, N.M. (2004). Influence of acute exercise on postprandial lipemia and endothelial dysfunction in normal- and overweight men. *Medicine and Science in Sport and Exercise***, 36(5)**, S218.

Hasbum, B., Real, J.T., Sánchez, C., Priego, M.A., Díaz, J., Viguer, A., Basanta, M., Martínez-Valls, J., Marín, J., Carmena, R., Ascaso, J.F. (2006). Effects of a controlled program of moderate physical exercise on insulin sensitivity in nonobese, nondiabetic subjects. *Clinical Journal of Sport Medicine*, **16(1)**, 46-50.

Haskell, W.L. (1986). The influence of exercise training on plasma lipids and lipoproteins in health and disease. *Acta Medica Scandinavica Supplement*, **711**, 25-37.

Haskell, W.L., Lee, I.M., Pate, R.R., Powell, K.E., Blair, S.N., Franklin, B.A., Macera, C.A., Heath, G.W., Thompson, P.D., Bauman, A. (2007). Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Medicine and Science in Sports and Exercise*, **39(8)**, 1423-1434.

Haslam, D.W., James, W.P. (2005). Obesity. *Lancet*, **366(9492)**, 1197-1209.

Heilbronn, L.K., Noakes, M., Clifton, P.M. (2001). Energy restriction and weight loss on very-low-fat diets reduce C-reactive protein concentrations in obese, healthy women. *Arteriosclerosis Thrombosis and Vascular Biology,* **21**, 968–970.

Heitmann, B.L., Lissner, L. (1995). Dietary underreporting by obese individuals – is it specific or non-specific? *BMJ,* **311**, 986-989.

Henriksen, E.J., Halseth, A.E. (1994). Early alterations in soleus GLUT-4, glucose transport, and glycogen in voluntary running rats. *Journal of Applied Physiology,* **76**, 1862-1867.

Herd, S.L., Lawrence, J.E., Malkova, D., Murphy, M.H., Mastana, S., Hardman, A.E. (2000). Postprandial lipemia in young men and women of contrasting training status. *Journal of Applied Physiology,* **89(5)**, 2049-2056.

Herman, C.P., Polivy, J. (2005). Normative influences on food intake. *Physiology and Behaviour,* **86**, 762-772.

Hevener, A.L., Reichart, D., Olefsky, J. (2000). Exercise and thiazolidinedione therapy normalize insulin action in the obese Zucker fatty rat. *Diabetes,* **49**, 2154-2159.

Higashi, Y., Sasaki, S., Kurisu, S., et al., (1999) Regular aerobic exercise augments endotheliumdependent vascular relaxation in normotensive as well as hypertensive subjects. *Circulation*, **100**, 1194-1202.

Hill, R.J., Davies, P.S.W. (2001). The validity of self-reported energy intake as determined using the doubly labelled water technique. *British Journal of Nutrition*, **85**, 415-430.

Hise, M.E., Sullivan, D.K., Jacobsen, D.J., Johnson, S.L., Donnelly, J.E. (2002). Validation of energy intake measurements determined from observer-recorded food records and recall methods compared with the doubly labeled water method in overweight and obese individuals. *American Journal of Clinical Nutrition*, **75(2)**, 263-267.

Ho, J.K., Duclos, R.I. Jr, Hamilton, J.A. (2002). Interactions of acyl carnitines with model membranes: a (13)C-NMR study. *Journal of Lipid Research*, **43**, 1429–1439.

Hoetzer, G.L., Van Guilder, G.P., Irmiger, H.M., Keith, R.S., Stauffer, B.L., DeSouza, C.A. (2007). Aging, exercise, and endothelial progenitor cell clonogenic and migratory capacity in men. *Journal of Applied Physiology*, **102(3)**, 847-852.

Holcomb, C.A., Heim, D.L., Loughin, T.M. (2004). Physical activity minimizes the association of body fatness with abdominal obesity in white, premenopausal women:

results from the Third National Health and Nutrition Examination Survey. *Journal of American Dietetic Association*, **104(12)**, 1859-1862.

Holloszy, J.O. (2005). Exercise-induced increase in muscle insulin sensitivity. *Journal of Applied Physiology*, **99**, 338-343.

Horowitz, J.F. (2007). Exercise-induced alterations in muscle lipid metabolism improve insulin sensitivity. *Exercise and Sport Science Reviews*. **35(4)**, 192-196.

Hope, S.A., Meredith, I.T. (2003). Cellular adhesion molecules and cardiovascular disease. Part I. Their expression and role in atherogenesis. *International Medical Journal*, **33**, 380-386.

Houmard, J.A., Tanner, C.J., Slentz, C.A., Duscha, B.D., McCartney, J.S., Kraus, W.E. (2004). Effect of the volume and intensity of exercise training on insulin sensitivity. *Journal of Applied Physiology*, **96(1)**, 101-106.

Hu, F.B., Sigal, R.J., Rich-Edwards, J.W., Colditz, G.A., Solomon, C.G., Willett, W.C., Speizer, F.E., Manson, J.E. (1999). Walking compared with vigorous physical activity and risk of type 2 diabetes in women: a prospective study. *JAMA*, **282(15)**, 1433-1439.

Hu, G., Qiao, Q., Silventoinen, K., Eriksson, J.G., Jousilahti, P., Lindström, J., Valle, T.T., Nissinen, A., Tuomilehto, J. (2003). Occupational, commuting, and leisure-time

physical activity in relation to risk for Type 2 diabetes in middle-aged Finnish men and women. *Diabetologia*, **46(3)**, 322-329.

Hubert, P. (1998). Uncoupling the effects of energy expenditure and energy intake: appetite response to short-term energy deficit induced by meal omission and physical activity. *Appetite*, **31**, 9-19.

Huffman, K.M., Samsa, G.P., Slentz, CA., et al., (2006) Response of high-sensitivity C-reactive protein to exercise training in an at-risk population. *American Heart Journal*, **152**, 793-800.

Hyson, D., Rutledge, J.C., Berglund, L. (2003). Postprandial lipemia and cardiovascular disease. *Current Atherosclerosis Reports*, **5**, 437-444.

Imbeault, P., Saint-Pierre, S., Almeras, N., Tremblay, A. (1997). Acute effects of exercise on energy intake and feeding behaviour. *British Journal of Nutrition*, **77**, 511-521.

Institute of Medicine of the National Academies of Science. (2002). Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids (macronutrients). Washington, DC: National Academy Press.

Irwin, M.L, Yasui, Y., Ulrich, C.M., Brown, D., Rudolph, R.E., Schwartz, R.S., Yukawa, M., Aiello, E., Potter, J.D., McTiernan, A. (2003). Effect of exercise on total and intra-abdominal body fat in postmenopausal women. *JAMA*, **298**, 323-330.

Jagla, A., Schrezenmeir, J. (2001). Postprandial triglycerides and endothelial function. *Experimental and Clinical Endocrinology and Diabetes*, **109**, S533-S547.

Jakicic, J.M., Wing, R.R., Butler, B.A., Robertson, R.J. (1995). Prescribing exercise in multiple short bouts versus one continuous bout: effects on adherence, cardiorespiratory fitness, and weight loss in overweight women. *International Journal of Obesity and Related Metabolic Disorders*, **19(12)**, 893-901.

Jakicic, J.M., Winters, C., Lang, W., Wing, R.R. (1999). Effects of intermittent exercise and use of home exercise equipment on adherence, weight loss, and fitness in overweight women: a randomized trial. *JAMA*, **282(16)**, 1554-1560.

Jakicic, J.M., Clark, K., Coleman, E., Donnelly, J.E., Foreyt, J., Melanson, E., Volek, J., Volpe, S.L. (2001). ACSM position stand on the appropriate intervention strategies for weight loss and prevention of weight regain for adults. *Medicine and Science in Sports and Exercise*, **33(12),** 2145-2156.

Jebb, S.A., Moore, M.S. (1999). Contribution of a sedentary lifestyle and inactivity to the aetiology of overweight and obesity: current evidence and research issues. *Medicine and Science in Sports and Exercise*, **31(11)**, S534-541.

Jebb, S.A., Cole, T.J., Doman, D., Murgatroyd, P.R., Prentice, A.M. (2000). Evaluation of the novel Tanita body-fat analyser to measure body composition by comparison with a four-compartment model. *British Journal of Nutrition*, **83**, 115-122.

Jeffery, R.W., Wing, RR., Sherwood, N., Tate D. (2003). Physical activity and weight loss: does prescribing higher physical activity goals improve outcome? *American Journal of Clinical Nutrition*, **78**, 684-689.

Johnson, R.K. (2002). Dietary Intake – How do we measure what people are really eating? *Obesity Research,* **10**, 63S – 68S.

Jones, W.H.S. (1967). Hippocrates (translated by W.H.S Jones). Cambridge, MA: Harvard University Press.

Jordan, J., Beneke, R., Hutler, M., Veith, A., Haller, H., Luft, F.C. (1997). Moderate exercise leads to decreased expression of beta1 and beta2 integrins on leucocytes. *European Journal of Applied Physiology and Occupational Physiology*, **76**, 192– 194.

Kadoglou, N.P., Iliadis, F., Angelopoulou, N., Perrea, D., Ampatzidis, G., Liapis, C.D., Alevizos, M. (2007). The anti-inflammatory effects of exercise training in patients with type 2 diabetes mellitus. *European Journal of Cardiovascular Prevention and Rehabilitation*, **14(6)**, 837-843.

Karpe, F. (1999). Postprandial lipoprotein metabolism and atherosclerosis. *Journal of Internal Medicine*, **246(4)**, 341-355.

Kasapis, C., Thompson, P.D. (2005). The effects of physical activity on serum C-reactive protein and inflammatory markers. A systematic review. *Journal of American College of Cardiology*, **45**, 1563-1569.

Katz, D.L., O'Connell, M., Yeh, M.C., Nawaz, H., Njike, V., Anderson, L.M., Cory, S., Dietz, W. (2005). Public health strategies for preventing and controlling overweight and obesity in school and worksite settings: a report on recommendations of the Task Force on Community Preventive Services. *Recommendations and Reports*, **54(10)**, 1-12.

Katzmarzyk, P.T., Church, T.S., Janssen, I., Ross, R., Blair, S.N. (2005). Metabolic syndrome, obesity, and mortality: impact of cardiorespiratory fitness. *Diabetes Care*, **28(2)**, 391-397.

Katzmarzyk, P.T., Janssen, I., Ross, R., Church, T.S., Blair, S.N. (2006). The importance of waist circumference in the definition of metabolic syndrome: prospective analyses of mortality in men. *Diabetes Care*, **29(2)**, 404-409.

Keim, N.L., Barbieri, T.F., Belko, A.Z. (1990). The effect of exercise on energy intake and body composition in overweight women. *International Journal of Obesity*, **14(4)**, 335-346.

Keim, N.L., Canty, D.J, Barbieri, T.F., Wu, M.M. (1996). Effect of exercise and dietary restraint on energy intake of reduced-obese women. *Appetite,* **26**, 55-70.

Keith, S.W., Redden, D.T., Katzmarzyk, P.T., Boggiano, M.M., Hanlon, E.C., Benca, R.M., Ruden, D., Pietrobelli, A., Barger, J.L., Fontaine, K.R., et al., (2006). Putative contributors to the secular increase in obesity: exploring the roads less travelled. *International Journal of Obesity*, **30(11)**, 1585-1594.

Keller, C., Keller, P., Giralt, M., Hidalgo, J., Pedersen, B.K. (2004). Exercise normalises overexpression of TNF-alpha in knockout mice. *Biochemical and Biophysical Research Communications*, **321**, 179–182.

Kelley, D.E., Goodpaster, B.H. (1999). Effects of physical activity on insulin action and glucose tolerance in obesity. *Medicine and Science in Sports and Exercise*, **31**, S619-S623.

Kempen, K., Saris, W.H.M., Westerterp, K. (1995). Energy balance during an 8-wk energy –restricted diet with and without exercise in obese women. *American Journal of Clinical Nutrition*, **62**, 722-729.

Kennedy, J.W., Hirshman, M.F., Gervino, E.V., Ocel, J.V., Forse, R.A., Hoenig, S.J., Aronson, D., Goodyear, L.J., Horton, E.S. (1999). Acute exercise induces GLUT4 translocation in skeletal muscle of normal human subjects and subjects with type 2 diabetes. *Diabetes*, **48**, 1192-1197.

Kesaniemi, Y.K., Danforth, E., Jensen, M.D., Kopelman, P.G., Lefebvre, P., Reeder , B.A. (2001). Dose response issues concerning physical activity and health: an evidence-based symposium. *Medicine and Science in Sports and Exercise*, **33(6)**, S351-358.

Kim, E.S., Im, J.A., Kim, K.C., Park, J.H., Suh, S.H., Kang, E.S., Kim, S.H., Jekal, Y., Lee, C.W., Yoon, Y.J., Lee, H.C., Jeon, J.Y. (2007). Improved insulin sensitivity and adiponectin level after exercise training in obese Korean youth. *Obesity (Silver Spring)*, **15(12)**, 3023-3030.

King, D.E., Carek, P., Mainous, A.G. III, Pearson, W.S. (2003). Inflammatory markers and exercise: differences related to exercise type. *Medicine and Science in Sports and Exercise*, **35**, 575–581.

King, J.A., Wasse, L.K., Broom, D.R., Stensel, D.J. (2010a). Influence of brisk walking on appetite, energy intake, and plasma acylated ghrelin. *Medicine and Science in Sports and Exercise*, **42(3)**, 485-492.

King, J.A., Miyashita, M., Wasse, L.K., Stensel, D.J. (2010b). Influence of prolonged treadmill running on appetite, energy intake and circulating concentrations of acylated ghrelin. *Appetite*, **in print**

King, N.A., Burley, V.J., Blundell, J.E. (1994). Exercise –induced suppression of appetite: effects on food intake and implications for energy balance. *European Journal of Clinical Nutrition*, **48**, 715-724.

King, N.A., Blundell, J.E. (1995). High-fat foods overcome the energy expenditure induced by high-intensity cycling or running. *European Journal of Clinical Nutrition*, **49(2)**, 114-123.

King, N.A., Snell, L., Smith, R.D., Blundell, J.E. (1996). Effects of short-term exercise on appetite responses in unrestrained females. *European Journal of Clinical Nutrition*, **50(10)**, 663-667.

King, N.A., Lluch, A., Stubbs, R.J., Blundell, J.E. (1997a). High dose exercise does not increase hunger or energy intake in free living males. *European Journal of Clinical Nutrition*, **51**, 478-483.

King, N.A., Tremblay, A., Blundell, J.E. (1997b). Effects of exercise on appetite control: implications for energy balance. *Medicine and Science in Sports and Exercise*, **29**, 1076-1089.

King, N.A., Caudwell, P., Hopkins, M., Byrne, N.M., Colley, R., Hills, A.P., Stubbs, J.R., Blundell, J.E. (2007). Metabolic and behavioural compensatory responses to exercise interventions: barriers to weight loss. *Obesity*, **15**, 1373-1383.

King, N.A., Hopkins, M., Caudwell, P., Stubbs, R.J., Blundell, J.E. (2008). Individual variability following 12 weeks of supervised exercise: identification and characterization of compensation for exercise-induced weight loss. *International Journal of Obesity*, **32**, 177-184.

King, N.A., Caudwell, P.P., Hopkins, M., Stubbs, J.R., Naslund, E., Blundell, J.E. (2009a). Dual-process action of exercise on appetite control: increase in orexigenic drive but improvement in meal-induced satiety. *American Journal of Clinical Nutrition*, **90(4)**, 921-927.

King, N.A., Hopkins, M., Caudwell, P., Stubbs, R.J., Blundell, J.E. (2009b). Beneficial effects of exercise: shifting the focus from body weight to other markers of health. *British Journal of Sports Medicine*, **43(12)**, 924-927.

Kingwell, B. A., Sherrard, B., Jennings, G. L. and Dart, A. M. (1997). Four weeks of cycle training increases basal production of nitric oxide from the forearm. *American Journal of Physiology*, **272**, H1070–H1077.

Kirkby, J., Metcalf, B.S., Jeffery, A.N., O'Riordan, C.F., Perkins, J., Voss, L.D., Wilkin, T.J. (2004). Sex differences in resting energy expenditure and their relation to insulin resistance in children (EarlyBird 13). *American Journal of Clinical Nutrition*, **80(2)**, 430-435.

Kissileff, H., Pi-Sunyer, F., Segal, K., Meltzer, S., Foelsch, P.A. (1990). Acute effects of exercise on food intake in obese and nonobese women. *American Journal of Clinical Nutrition*, **52**, 240-245.

Klausen, B., Toubro, S., Ranneries, C., Rehfeld, J.F., Holst, J.J., Christensen, N.J., Astrup, A. (1999). Increased intensity of a single exercise bout stimulates subsequent fat intake. *International Journal of Obesity*, **23**, 1282-1287.

Klein, S., Fontana, L., Young, V.L., Coggan, A.R., Kilo, C., Patterson, B.W., Mohammed, B.S. (2004). Absence of an effect of liposuction on insulin action and risk factors for coronary heart disease. *New England Journal of Medicine*, **350(25)**, 2549-2557.

Knowler, W.C., Barrett-Connor, E., Fowler, S.E., Hamman, R.F., Lachin, J.M., Walker, E.A., Nathan, D.M., Diabetes Prevention Program Research Group. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *New England Journal of Medicine*, **346(6)**, 393-403.

Kobayashi, N., Tsuruya, Y., Iwasawa, T., et al., (2003). Exercise training in patients with chronic heart failure improves endothelial function predominantly in the trained extemities. *Circulation Journal*, **67**, 505-510.

Kolifa, M., Petridou, A., Mougios, V. (2004). Effect of prior exercise on lipemia after a meal of moderate fat content. *European Journal of Clinical Nutrition*, **58(10)**, 1327-1335.

Kokalas, N., Petridou, A., Nikolaidis, M.G., Mougios, V. (2005). Effect of aerobic exercise on lipaemia and its fatty acid profile after a meal of moderate fat content in eumenorrhoeic women. *British Journal of Nutrition*, **94(5)**, 698-704.

Kopp, H.P., Kopp, C.W., Festa, A., et al., (2003). Impact of weight loss on inflammatory proteins and their association with the insulin resistance syndrome in morbidly obese patients. *Arteriosclerosis Thrombosis and Vascular Biology*, **23**, 1042–1047.

Kraus, W.E., Houmard, J.A., Duscha, B.D., et al., (2002). Effects of the amount and intensity of exercise on plasma lipoproteins. *New England Journal of Medicine*, **347**, 1483-1492.

Kruger, J., Galuska, D., Serdula, M., Jones, D. (2004). Attempting to lose weight, specific practices among US adults. *American Journal of Preventive Medicine*, **26(5)**, 402-406.

Lakka, T.A., Lakka, H.M., Rankinen, T., Leon, A.S., Rao, D.C., Skinner, J.S., Wilmore, J.H., Bouchard, C. (2005). Effect of exercise training on serum levels of C-reactive protein in healthy individuals: the HERITAGE Family Study. *European Heart Journal*, **26**, 2018-2025.

Lalonde, L., Gray-Donald, K., Lowensteyn, I., **et al**. (2002). Comparing the benefits of diet and exercise in the treatment of dyslipidemia. *Preventive Medicine*, **35**, 16–24.

Lamarche, B., Després, J.P., Pouliot, M.C., Moorjani, S., Lupien, P.J., Thériault, G., Tremblay, A., Nadeau, A., Bouchard, C. (1992). Is body fat loss a determinant factor in the improvement of carbohydrate and lipid metabolism following aerobic exercise training in obese women? *Metabolism*, **41(11)**, 1249-1256.

LaMonte, M.J., Blair, S.N., Church, T.S. (2005). Physical activity and diabetes prevention. *Journal of Applied Physiology*, **99(3)**, 1205-1213.

Landmesser, U., Hornig, B., Drexler, H. (2004). Endothelial function. A critical determinant in atherosclerosis? *Circulation*, **109**, II-27-II-33.

Lanes, R., Paoli, M., Carrillo, E., Villaroel, O., Palacios, A. (2004). Peripheral inflammatory and fibrinolytic markers in adolescents with growth hormone deficiency: relation to postprandial lipemia. *Journal of Pediatrics*, **145**, 657-661.

Lau, D.C., Obesity Canada Clinical Practice Guidelines Steering Committee and Expert Panel. (2007). Synopsis of the 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children. *CMAJ*, **176(8)**, 1103-1106.

Lazzer, S., Boirie, Y., Bitar, A., Montaurier, C., Vernet, J., Meyer, M., Vermorel, M. (2003). Assessment of energy expenditure associated with physical activities in free-living obese and nonobese adolescents. *American Journal of Clinical Nutrition.* **78(3)**, 471-479.

Lebovitz, H.E., Banerji, M.A. (2005). Point: visceral adiposity is causally related to insulin resistance. *Diabetes Care*, **28(9)**, 2322-2325.

Lee, C.D., Blair, S.N., Jackson, A.S. (1999). Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. *American Journal of Clinical Nutrition*, **69(3)**, 373-380.

Leeuwenberg, J., Smeets, E., Neefjes, J., et al., (1992). E-selectin and intercellular adhesion molecule-1 are released by activated human endothelial cells in vitro. *Immunology*, **77(4)**, 543-549.

Leon, A.S., Conrad, J., Hunninghake, D.B., Serfass, R. (1979). Effects of a vigorous walking program on body composition, and carbohydrate and lipid metabolism of obese young men. *American Journal of Clinical Nutrition*, **32(9)**, 1776-1787.

Leon, A.S. (1987). Age and other predictors of coronary heart disease. *Medicine and Science in Sports and Exercise*, **19(2)**, 159-167.

Leon, A.S., Casal, D., Jacobs, D.R.J. (1996). Effects of 2,000 kcal per week of walking and stair climbing on physical fitness and risk factors for coronary heart disease. *Journal of Cardiopulmonary Rehabilitation*, **16(3)**, 183-192.

Leon, A.S., Sanchez, O.A. (2001). Response of blood lipids to exercise training alone or combined with dietary intervention. *Medicine and Science in Sports and Exercise*, **33(6)**, S502-515; discussion S528-9.

Levine, J.A., Eberhardt, N., Jense, M. (1999). Leptin responses to overfeeding: Relationship with body fat and nonexercise activity thermogenesis. *Journal of Clinical Endocrinology and Metabolism*, **84(8)**, 2751-2754.

Levine, J.A. (2005). Measurement of energy expenditure. *Public Health Nutrition*, **8**, 1123-1132.

Levine, J.A., Kotz C. (2005). NEAT- non-exercise activity thermogenesis- egocentric and geocentric environmental factors vs biological regulation. *Acta Physiologica Scandinavica*, **184**, 309-318.

Libby, P. (2002). Inflammation in atherosclerosis. *Nature*, **440**, 868-874.

Lloyd-Jones, D.M., Liu, K., Colangelo, L.A., et al., (2007). Consistently stable or decreased body mass index in young adulthood and longitudinal changes in metabolic syndrome components: the Coronary Artery Risk Development in Young Adults Study. *Circulation*, **115,** 1004–1011.

Lluch, A., King, N.A., Blundell, J.E. (1998). Exercise in dietary restrained women: no effect on energy intake but change in hedonic ratings. *European Journal of Clinical Nutrition*, **52**, 300-307.

Lluch, A., King, N.A., Blundell, J.E. (2000). No energy compensation at the meal following exercise in dietary restrained and unrestrained women. *British Journal of Nutrition*, **84(2)**, 219-225.

Long, Y.C., Widegren, U., Zierath, J.R. (2004). Exercise- induced mitogen –activated protein kinase signalling in skeletal muscle. *Proceedings of Nutrition Society*, **63**, 227-232.

Loos, R.J.F., Bouchard, C. (2003). Obesity: is it a genetic disorder? *Journal of Internal Medicine*, **254**, 401-425.

Lovejoy, J.C., Sainsbury, A., Stock Conference 2008 Working Group. (2009). Sex differences in obesity and the regulation of energy homeostasis. *Obesity Reviews*, **10(2**), 154-167.

Lynch, J., Helmrich, S.P., Lakka, T.A., Kaplan, G.A., Cohen, R.D., Salonen, R., & Salonen, J.T. (1996). Moderately intense physical activities and high levels of cardiorespiratory fitness reduce risk of Non-Insulin-Dependent Diabetes Mellitis in middle-aged men. *Archives of Internal Medicine*, **156**, 1307-1314.

Magkos, F., Mohammed, B.S., Mittendorfer, B. (2010). Enhanced insulin sensitivity after acute exercise is not associated with changes in high-molecular weight adiponectin concentration in plasma. *European Journal of Endocrinology*, **162(1)**, 61-66.

Malkova, D., Hardman, A.E., Bowness, R.J., MacDonald, I.A. (1999). The reduction in postprandial lipemia after exercise is independent of the relative contributions of fat and carbohydrate to energy metabolism during exercise. *Metabolism*, **48(2)**, 245-251.

Malkova, D., Evans, R.D., Frayn, K.N., Humphreys, S.M., Jones, P.R., Hardman, A.E. (2000). Prior exercise and postprandial substrate extraction across the human leg. *American Journal of Physiology Endocrinology and Metabolism*, **279(5)**, E1020-1028.

Malkova, D., Gill, J.M.R. (2006). Effects of exercise on postprandial lipoprotein metabolism. *Future lipidology*, **1(6)**, 743-755.

Malkova, D., McLaughlin, R., Manthou, E., Wallace, A.M., Nimmo, M.A. (2008). Effect of moderate-intensity exercise session on preprandial and postprandial responses of circulating ghrelin and appetite. *Hormonal and Metabolic Research*, **40(6)**, 410-415.

Maraki, M., Tsofliou, F., Pitsiladis, Y.P., Malkova, D., Mutrie, N., Higgins, S. (2005). Acute effects of a single exercise class on appetite, energy intake and mood. Is there a time of day effect? *Appetite*, **45**, 272-278.

Marcell, T.J., McAuley, K.A., Traustadottir, T., Reaven, P.D. (2005). Exercise training is not associated with improved levels of C-reactive protein or adiponectin. *Metabolism*, **54**, 533-541.

Marfell-Jones, M., Olds, T., Stewart, A., Carter, L. (2006). International standards for anthropometric assessment. Potchefstroom, South Africa: ISAK.

Martins, C., Morgan, L.M., Bloom, S.R., Robertson, M.D. (2007a). Effects of exercise on gut peptides, energy intake and appetite. *Journal of Endocrinology*, **193(2)**, 251-258.

Martins, C., Truby, H., Morgan, L.M. (2007b). Short-term appetite control in response to a 6-week exercise programme in sedentary volunteers. *British Journal of Nutrition*, **98(4)**, 834-842.

Martins, C., Morgan, L., Truby, H. (2008). A review of the effects of exercise on appetite regulation: an obesity perspective. *International Journal of Obesity*, **32(9)**, 1337-1347.

Martins, C., Kulseng, B., King, N.A., Holst, J.J., Blundell, J.E. (2010). The effects of exercise-induced weight loss on appetite-related peptides and motivation to eat. *Journal of Clinical Endocrinology and Metabolism*, **in press.**

Melzer, K., Kayser, B., Saris, W.H., Pichard, C. (2005). Effects of physical activity on food intake. *Clinical Nutrition*, **24(6)**, 885-895.

Matthews, D.R., Hosker, J.P., Rudenski, A.S., Naylor, B.A., Treacher, D.F., Turner, R.C. (1985). Homeostasis model assessment: insulin resistance and B cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*, **28**, 412-419.

Matthys, P., Mitera, T., Heremans, H., Van Damme, J., Billiau, A. (1995). Anti-gamma interferon and anti-interleukin-6 antibodies affect staphylococcal enterotoxin B-induced weight loss, hypoglycemia, and cytokine release in D-galactosamine-sensitized and unsensitized mice. *Infection and Immunity*, **63**, 1158–1164.

Mattusch, F., Dufaux, B., Heine, O., Mertens, I., Rost, R. (2000). Reduction of the plasma concentration of C-reactive protein following nine months of endurance training. *International Journal of Sports Medicine*, **21**, 21–24.

Maughan, R.J. (1982). A simple, rapid method for the determination of glucose, lactate, pyruvate, alanine, 3-hydroxybutyrate and acetoacetate on a single 20-l blood sample. *Clinica Chimica Acta*, **122**, 231-240.

Mayers, J., Marshall, N.B., Vitale, J.J., Christensen, J.H., Mashayekhi, M.B., Stare, F.J. (1954). Exercise food intake and body weight in normal rats and genetically obese adult mice. *American Journal of Physiology*, **177(3)**, 544-548.

McLaughlin, R., Malkova, D., Nimmo, M.A. (2006). Spontaneous activity responses to exercise in males and females. *European Journal of Clinical Nutrition*, **60**, 1055-1061.

Melzer, K., Kayser, B., Saris, W.H.M., Pichard, C. (2005). Effects of physical activity on food intake. *Clinical Nutrition*, **24**, 885–895.

Menshikova, E.V., Ritov, V.B., Fairfull, L., Ferrell, R.E., Kelley, D.E., Goodpaster, B.H. (2006). Effects of exercise on mitochondrial content and function in aging human skeletal muscle. *Journal of Gerontological and Biological Science in Medicine Science*, **61**, 534–540.

Mertens, D.J., Kavanagh, T., Campbell, R.B., Shephard, R.J. (1998). Exercise without dietary restriction as a means to long-term fat loss in the obese cardiac patient. *Journal of Sports Medicine and Physical Fitness*, **38(4)**, 310-316.

Mestek, M.L. (2009). Physical activity, blood lipids, and lipoproteins. *American Journal of Lifestyle Medicine*, **3**, 279.

Meydani, M. (2003). Soluble adhesion molecules: surrogate markers of cardiovascular disease? *Nutrition Reviews*, **61**, 63-68.

Mikines, K.J., Sonne, B., Farrell, P.A., Tronier, B., Galbo, H. (1988). Effect of physical exercise on sensitivity and responsiveness to insulin in humans. *American Journal of Physiology*, **254(3)**, E248-259.

Milani, R.V., Lavie, C.J., Mehra, M.R. (2004). Reduction in C-reactive protein through cardiac rehabilitation and exercise training. *Journal of American College of Cardiology*, **43**, 1056-1061.

Miller, W.C., Koceja, D.M., Hamilton, E.J. (1997). A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention. *International Journal of Obesity and Related Metabolic Disorders,* **21**, 941-947.

Minderico, C.S., Silva, A.M., Keller, K., Branco, T.L., Martins, S.S, Palmeira, A.L., et al., (2008). Usefulness of different techniques for measuring body composition changes during weight loss in overweight and obese women. *British Journal of Nutrition*, **99(2)**, 432-441.

Mohammed, B.S., Cohen, S., Reeds, D., Young, V.L., Klein, S. (2008). Long-term effects of large-volume liposuction on metabolic risk factors for coronary heart disease. *Obesity (Silver Spring)*. **16(12)**, 2648-2651.

Moncada, S., Higgs, A. (1993). Mechanisms of disease: the L-arginine-nitric oxide pathway. *New England Journal of Medicine*, **329(27)**, 2002-2012.

Moon, J.K., Butte, N.F. (1996). Combined heart rate and activity improve estimates of oxygen consumption and carbon dioxide production rates. *Journal of Applied Physiology*, **81,** 1754-1761.

Morris, J.N., Heady, J.A., Raffle, P.A.B., Parks, J.W., Roberts, C.G. (1953). Coronary heart disease and physical activity work. *The Lancet*, **1053-7**, 1111-1120.

Moyna, N., Estrada, E., LaRocca, G.M., et al., (2001). Endothelial function in adolescents with type 2 diabetes. *Medicine and Science in Sport and Exercise*, **33(5)**, S395.

Moyna, N., Thompson, P.D. (2004). The effect of physical activity on endothelial function in man. Acta Physiologica Scandinavica, **(180)**, 113-123.

Müller-Riemenschneider, F., Reinhold, T., Berghöfer, A., Willich, S.N. (2008). Health-economic burden of obesity in Europe. *European Journal of Epidemiology*, **23(8)**, 499-509.

Nassis, G.P., Papantakou, K., Skenderi, K., Triandafillopoulou, M., Kavouras, S.A., Yannakoulia, M., Chrousos, G.P., Sidossis, L.S. (2005). Aerobic exercise training improves insulin sensitivity without changes in body weight, body fat, adiponectin, and inflammatory markers in overweight and obese girls. *Metabolism*, **54(11)**, 1472-1479.

Nassis, G.P., Sidossis, L.S. (2009). Thighs and heart disease. Exercise, muscle mass, and insulin sensitivity. *BMJ*, 339.

Neter, J.E., Stam, B.E., Kok, F.J., Grobbee, D.E., Geleijnse, J.M. (2003). Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. *Hypertension*, **42**, 878–884.

NHI Consensus Development Panel on Physical Activity and Cardiovascular Health. (1996). Physical activity and cardiovascular health. *JAMA*, **276**, 241–246.

Nicklas, B.J., You, T., Pahor, M. (2005). Behavioural treatments for chronic systemic inflammation: effects of dietary weight loss and exercise training. *CMAJ*, **172**,1199-1209.

Niebauer, J., Cooke, J.P. (1996). Cardiovascular effects of exercise: role of endothelial shear stress. *JACC*, **28(7)**, 1652-1660.

Nordestgaard, B.G., Benn, M., Schnohr, P., Tybjaerg-Hansen, A. (2007). Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women. *JAMA*, **298(3)**, 299-308.

Oguma, Y., Shinoda-Tagawa, T. (2004). Physical activity decreases cardiovascular disease risk in women:review and meta-analysis. *American Journal of Preventive Medicine*, **26**, 407–418.

Ostrowski, K., Hermann, C., Bangash, A., Schjerling, P., Nielsen, J.N., Pedersen, B.K. (1998). A trauma-like elevation of plasma cytokines in humans in response to treadmill running. *Journal of Physiology*, **513**, 889 –894.

Ostrowski, K., Rohde, T., Asp, S., Schjerling, P., Pedersen, B.K. (1999). Pro- and anti-inflammatory cytokine balance in strenuous exercise in humans. *Journal of Physiology*, **515**, 287–291.

Ostrowski, K., Rohde, T., Asp, S., Schjerling, P., Pedersen, B.K. (2001). Chemokines are elevated in plasma after strenuous exercise in humans. *European Journal of Applied Physiology*, **84**, 244 –245.

Paffenbarger, R.S., Hale, W.E. (1975). Work activity and coronary heart disease. *New England Journal of Medicine*, **292**, 545-550.

Paffenbarger, R.S. Jr, Hyde, R.T., Wing, A.L., Hsieh, C.C. (1986). Physical activity, all-cause mortality, and longevity of college alumni. *New England Journal of Medicine*, **314(10)**, 605-613.

Paffenbarger, R.S. Jr, Hyde, R.T., Wing, A.L., Lee, I.M., Jung, D.L., Kampert, J.B. (1993). The association of changes in physical-activity level and other lifestyle characteristics with mortality among men. *New England Journal of Medicine*, **328(8)**, 538-545.

Parati, G., Stergiou, G.S., Asmar, R., Bilo, G., de Leeuw, P., Imai, Y., Kario, K., Lurbe, E., Manolis, A., Mengden, T., et al., (2008). ESH Working Group on Blood Pressure Monitoring. European Society of Hypertension guidelines for blood pressure monitoring at home: a summary report of the Second International Consensus Conference on Home Blood Pressure Monitoring. *Journal of Hypertension*, **26(8)**, 1505-1526.

Pate, R.P., Pratt, M., Blair, S.N., Haskell, W.L., Macera, C.A., Bouchard, C., Buchner, D., Ettinger, W., Heath, G.W., King, A.C., et al. (1995). Physical activity ad public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA*, **273(5)**, 402-407.

Patsch, J.R., Miesenbock, G., Hopferweiser, T., et al., (1992). Relation of triglyceride metabolism and coronary artery disease: Studies in the postprandial state. *Arteriosclerosis and Thrombosis*, **12**, 1336-1345.

Patsch, W., Esterbauer, H., Foger, B., Patsch, J.R. (2000). Postprandial lipemia and coronary risk. *Current Atherosclerosis Reports*, **2**, 232-242.

Pavlou, K.N., Whatley, J.E., Jannace, P.W., DiBartolomeo, J.J., Burrows, B.A., Duthie, E.A., Lerman, R.H. (1989). Physical activity as a supplement to a weight-loss dietary regimen. *American Journal of Clinical Nutrition*, **49(5)**, 1110-1114.

Pearson, T.A., Mensah, G.A., Alexander, R.W., et al., (2003). Markers of inflammation and cardiovascular disease: appplication to clinical and public health practice: a statement for healthcare from the Centers for Disease Control and Prevention and the American Heart Association. *Circulation,* **107**, 499-511.

Perseghin, G., Price, T. B., Petersen, K. F., et al., (1996). Increased glucose transport-phosphorylation and muscle glycogen synthesis after exercise training in insulin-resistant subjects. *New England Journal of Medicine,* **335**, 1357–1362.

Perseghin, G., Ghosh, S., Gerow, K. and Shulman, G. I. (1997). Metabolic defects in lean nondiabetic offspring of NIDDM parents: a cross-sectional study. *Diabetes,* **46**, 1001–1009.

Petersen, A.M.W., Pedersen, B.K. (2005). The anti-inflammatory effect of exercise. *Journal of Applied Physiology,* **98**, 1154-1162.

Petersen, K.F., Shulman, G.I. (2002). Pathogenesis of skeletal muscle insulin resistance in type 2 diabetes mellitus. *American Journal of Cardiology*, **90(5A)**, 11G-18G.

Petitt, D.S., Cureton, K.J. (2003). Effects of prior exercise on postprandial lipemia: A quantitative review. *Metabolism*, **52(4)**, 418-424.

Phares, D.A., Halvestadt, A., Shuldiner, A.R., Ferrell, RE., Douglass, L.W., Ryan, A.S., Goldberg, A.P., Hagberg, J.M. (2004). Association between body fat response to exercise training and multilocus ADR genotypes. *Obesity Research*, **12**, 807-815.

Plotnick, G.D., Corretti, M.C., Vogel, R.A. (1997). Effect of antioxidant vitamins on the transient impairment of endothelium-dependent brachial artery vasoactivity following a single high-fat meal. *JAMA*, **278**, 1682-1686.

Pols, M.A., Peeters, P.H., Kemper, H.C., Collette, H.J. (1996). Repeatability and relative validity of two physical activity questionnaires in elderly women. *Medicine and Science in Sports and Exercise*, **28(8)**, 1020–1025.

Pomerleau, M., Imbeault, P., Parker, T., Doucet, E. (2004). Effects of exercise intensity on food intake and appetite in women. *American Journal of Clinical Nutrition*, **80**, 1230-1236.

Potteiger, J.A., Jacobsen, D.J., Donnelly, J.E., Hill, J.O. (2003). Midwest Exercise Trial. Glucose and insulin responses following 16 months of exercise training in overweight adults: the Midwest Exercise Trial. *Metabolism*, **52(9)**, 1175-1181.

Prentice, A.M., Jebb, S.A. (1995). Obesity in Britain: gluttony or sloth? *British Medical Journal*, **311(7002)**, 437-439.

Reaven, G. (1999). Syndrome X: 10 years after. Drugs. **58(1)**, 19-20; discussion 75-82.

Reger, W.E., Allison, T.A., Kurucz, R.L. (1984). Exercise, post-exercise metabolic rate and appetite. *Sports Health and Nutrition,* **2**, 115-123.

Rehman, J., Li, J., Parvathaneni, L., et al., (2004). Exercise acutely increases circulating endothelial progenitor cells and monocyte-/macrophage-derived angiogenic cells. *Journal of American College of Cardiology,* **43(12)**, 2314-2318.

Reichert, F.F., Barros, A.J., Domingues, M.R., Hallal, P.C. (2007). The role of perceived personal barriers to engagement in leisure-time physical activity. *American Journal of Public Health*. **97(3)**, 515-519.

Rennie, K.L., Coward, A., Jebb, S.A. (2007). Estimating under-reporting of energy intake in dietary surveys using an individualised method. *British Journal of Nutrition*. **97(6)**, 1169-1176.

Robert, F., Zoeller, Jr. (2007). Physical Activity and Obesity: Their Interaction and Implications for Disease Risk and the Role of Physical Activity in Healthy Weight Management. American Journal of Lifestyle Medicine, **1(6)**, 437-446.

Roden, M., Stingl, H., Chandramouli, V., Schumann, W. C., Hofer, A., Landau, B. R., Nowotny, P., Waldhausl, W., Shulman, G. I. (2000). Effects of free fatty acid elevation

on postabsorptive endogenous glucose production and gluconeogenesis in humans, *Diabetes*, **49(5)**, 701-707.

Rosenberg, D.E., Jabbour, S.A., Goldstein, B.J. (2005). Insulin resistance, diabetes and cardiovascular risk: approaches to treatment. *Diabetes Obesity and Metabolism*, **7(6)**, 642-653.

Ross, R. (1999). Atherosclerosis- an inflammatory disease. *New England Journal of Medicine*, **340**, 115–126.

Ross, R, D. Dagnone, P.J.H. Jones, H., Smith, A., Paddags, R., et al., (2000). Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men. *Annals of Internal Medicine*, **133(2)**, 92-103.

Ross, R., Freemen, J., Hudson R., Janssen I. (2002). Abdominal obesity, muscle composition in insulin resistance in premenopausal women. *Journal of Clinical Endocrinology and Metabolism*, **87(11)**, 5044-5051.

Ross, R. (2003). Does exercise without weight loss improve insulin sensitivity? *Diabetes Care*, **26(3)**, 944-945.

Ross, R., Janssen, I., Dawson, J., Kungl, A.M., Kuk, J.L., Wong, S.L. (2004). **et al**. Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. *Obesity Research*, **12**, 789–798.

Saengsirisuwan, V., Kinnick, T.R., Schmit, M.B., Henriksen, E.J. (2001). Interactions of exercise training and α-lipoic acid on glucose transport in obese Zucker rat. *Journal of Applied Physiology*, **91**, 145-153.

Saris, W.H., Blair, S.N., van Baak, M.A., Eaton, S.B., Davies, P.S., Di Pietro, L, Fogelholm, M., Rissanen, A., Schoeller, D., Swinburn, B., Tremblay, A., Westerterp, K.R., Wyatt. (2003). How much physical activity is enough to prevent unhealthy weight gain? Outcome of the IASO 1st Stock Conference and consensus statement. *Obesity Reviews*, **4(2)**, 101-114.

Schenk, S., Horowitz, J.F. (2007). Acute exercise increases triglyceride synthesis in skeletal muscle and prevents fatty-acid induced insulin resistance. *Journal of Clinical Investigation*, **117**, 1679-1689.

Schenk, S., Harber, M.P., Shrivastava, C.R., Burant, C.F., Horowitz, J.F. (2009). Improved insulin sensitivity after weight loss and exercise training is mediated by a reduction in plasma fatty acid mobilization, not enhanced oxidative capacity. *Journal of Physiology*, **587(20)**, 4949-4961.

Schmidt, A., Pleiner, J., Bayerle-Eder, M., et al., (2002). Regular physical exercise improves endothelial function in heart transplant recipients. *Clinical Transplantion*, **16**, 137-143.

Schneider, K.L., Spring, B., Pagoto, S.L. (2008). Exercise and energy intake in overweight, sedentary individuals. *Eating Behaviour*, **10(1)**, 29-35.

Schneider, S.H., Amorosa, L.F., Khachadurian, A.K., Ruderman, N.B. (1984). Studies on the mechanism of improved glucose control during regular exercise in type 2 (non-insulin-dependent) diabetes. *Diabetologia*, **26(5)**, 355-360.

Schoeller, D.A. (1995). Limitations in the Assessment of dietary energy intake by self-report. *Metabolism*, **44(2)**, 18-22.

Schoeller, D.A., Shay, K., Kushner, R.F. (1997). How much physical activity is needed to minimize weight gain in previously obese women? *American Journal of Clinical Nutrition*, **66(3)**, 551-556.

Schoeller, D.A. (2008). Insights into energy balance from doubly labeled water. *International Journal of Obesity*, **32(7)**, S72-75.

Seale, J.L., Rumpler, W.V., Conway, J.M., Miles, C. W. (1990). Comparison of doubly labelled water, intake-balance, and direct- and indirect-calorimetry methods for

measuring energy expenditure in adult men. *American Journal of Clinical Nutrition*, **52**, 66-71.

Seale, J.L. (1995). Energy expenditure measurements in relation to energy requirements. *American Journal of Clinical Nutrition*, **62(5)**, 1042S-1046S.

Seidell, J.C. (2005). Epidemiology of obesity. *Seminars in Vascular Medicine*, **5(1)**, 3-14.

Seip, R., Mair, K., Cole, T.G., Semenkovich, C.F. (1997). Induction of human skeletal muscle lipoprotein lipase gene expression by short-term exercise is transient. *American Journal of Physiology Endocrinology and Metabolism*, **272**, E255-E261.

Shojaee-Moradie, F., Baynes, K.C., Pentecost, C., Bell, J.D., Thomas, E.L., Jackson, N.C., Stolinski, M., Whyte, M., Lovell, D., Bowes, S.B., et al., (2007). Exercise training reduces fatty acid availability and improves the insulin sensitivity of glucose metabolism. *Diabetologia*, **50(2)**, 404-13.

Shorten, A.L., Wallman, K.E., Guelfi, K.J. (2009). Acute effect of environmental temperature during exercise on subsequent energy intake in active men. *American Journal of Clinical Nutrition*, **90(5)**,1215-1221.

Silventoinen, K., Sans, S., Tolonen, H., Monterde, D., Kuulasmaa, K., Kesteloot, H., Tuomilehto, J., WHO MONICA Project. (2004). Trends in obesity and energy supply in the WHO MONICA Project. *International Journal of Obesity and Related Metabolic Disorders*, **28(5)**, 710-718.

Slentz, C.A., Duscha, B.D., Johnson, J.L., Ketchum, K., Aiken, L.B., Samsa, G.P., et al., (2004). Effects of amount of exercise on body weight body composition and measures of central obesity. STRRIDE- a randomized controlled study. *Archives of Internal Medicines*, **164(1)**, 31-39.

Smith, J.K., Dykes, R., Douglas, J.E., Krishnaswamy, G., Berk, S. (1999). Long-term exercise and atherogenic activity of blood mononuclear cells in persons at risk of developing ischemic heart disease. *JAMA*, **281**, 1722–1727.

Snyder, K.A., Donnelly, J.E., Jabobsen, D.J., Hertner, G., Jakicic, J.M. (1997). The effects of long-term, moderate intensity, intermittent exercise on aerobic capacity, body composition, blood lipids, insulin and glucose in overweight females. *International Journal of Obesity and Related Metabolic Disorders*, **21(12)**, 1180-1189.

Solomon, T.P., Sistrun, S.N., Krishnan, R.K., Del Aguila, L.F., Marchetti, C.M., O'Carroll, S.M., O'Leary, V.B., Kirwan, J.P. (2008). Exercise and diet enhance fat oxidation and reduce insulin resistance in older obese adults. *Journal of Applied Physiology*, **104(5)**, 1313-1319.

Starkie, R., Ostrowski, S.R., Jauffred, S., Febbraio, M., Pedersen, B.K. (2003). Exercise and IL-6 infusion inhibit endotoxin-induced TNF-α production in humans. *FASEB Journal*, **17**, 884–886.

Staten, M.A. (1991). The effect of exercise on food intake in men and women. *American Journal of Clinical Nutrition,* **53**, 27-31.

Steen, M.S., Foianini, K.R., Youngblood, E.B., Kinnick, T.R., Jacob, S., Henriksen, E.J. (1999). Interactions of exercise training and ACE inhibition on insulin action in obese Zucker rats. *Journal Applied Physiology,* **86**, 2044-2051.

Steensberg, A., Fischer, C.P., Keller, C., Moller, K., Pedersen, B.K. (2003). IL-6 enhances plasma IL-1ra, IL-10, and cortisol in humans. *American Journal of Physiology Endocrinology and Metabolism,* **285**, E433–E437.

Stevens, V.J., Obarzanek, E., Cook, N.R., **et al.** (2001). Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, phase II. *Annals of Internal Medicine,* **134**, 1–11.

Stubbs, R.J., Sepp, A., Hughes, D.A., Johnstone, A.M., King, N., Horgan, G., Blundell, J.E. (2002a). The effect of graded levels of exercise on energy intake and balance in

free-living men, consuming their normal diet. *European Journal of Clinical Nutrition,* **56**, 129-140.

Stubbs, R.J., Sepp, A., Hughes, D.A., Johnstone, A.M., King, N., Horgan, G., Blundell, J.E. (2002b). The effect of graded levels of exercise on energy intake and balance in free-living women. *International Journal of Obesity and Related Metabolic Disorders,* **26**, 866-869.

Stubbs, R.J., Hughes, D.A., Johnstone, A.M., Horgan, G.W., King, N., Blundell, J.E. (2004a). A decrease in physical activity affects appetite, energy, and nutrient balance in lean men feeding ad libitum. *American Journal of Clinical Nutrition,* **79**, 62-69.

Stubbs, R.J., Hughes, D.A., Johnstone, A.M., Whybrow, S., Horgan, G.W., King, N., Blundell, J. (2004b). Rate and extent of compensatory changes in energy intake and expenditure in response to altered exercise and diet composition in humans. *AJP Regulatory Integrative and Comparative Physiology,* **286**, R350-R358.

Sturm, R., Wells, K.B. (1998). Does obesity contribute as much to mortality as poverty or smoking? *Public Health*, **115**, 229-235.

Stutts, WC. (2002). Physical activity determinants in adults. Perceived benefits, barriers, and self efficacy. *AAOHN Journal*, **50(11)**, 499-507.

Spurway, N. C. (1992). Aerobic exercise, anaerobic exercise and the lactate threshold. *British Medical Bulletin*, **48**, 569-591.

Statistics on Obesity, Physical Activity and Diet: England, January 2008. (2010). The NHS Information Centre, UK.

Strath, S.J., Swartz, A.M., Bassett, D.R. Jr, O'Brien, W.L., King, G.A., Ainsworth, B.E. (2000). Evaluation of heart rate as a method for assessing moderate intensity physical activity. *Medicine and Science in Sports and Exercise*, **32(9)**, S465-4670.

Suzuki, S., Urata, G., Ishida, Y., Kaneshisa, H., Yamamura, M. (1998). Influences of low intensity exercise on body composition, food intake and aerobic power of sedentary young females. *Applied Human Sciences*, **17**, 259-266.

Swan, G. (2004). Findings from the latest National Diet and Nutrition Survey. *Proceedings of Nutrition Society*, **63**, 505-512.

Taylor, C., Rogers, G., Goodman, C., et al., (1987). Hematologic, iron-related, and acute-phase protein responses to sustained strenuous exercise. *Journal of Applied Physiology*, **62**, 464 –469.

Tchernof, A., Nolan, A., Sites, C.K., Ades, P.A., Poehlman, E.T. (2002). Weight loss reduces C-reactive protein levels in obese postmenopausal women. *Circulation*, **105**, 564–569.

The Diabetes Prevention Program Research Group (2002). Reduction in the incidence of type II diabetes with lifestyle intervention or Metformin. *New England Journal of Medicine*, **346(6)**, 393-403.

The Scottish Health Survey 2008. (2009). Volume 1: Main Report. Scottish Government.

Thompson, D., Markovitch, D., Betts, J.A., Mazzatti, D., Turner, J., Tyrrell, R.M. (2010). Time course of changes in inflammatory markers during a 6-mo exercise intervention in sedentary middle-aged men: a randomized-controlled trial. *Journal of Applied Physiology*, **108(4)**, 769-779.

Thompson, D., Batterham, A.M., Markovitch, D., Natalie, C.D., Lund, A.J.S., Walhin, J.P. (2009). Confusion and conflict in assessing the physical activity status of middle-aged men, *Plos One*, **4(2).**

Thompson, D., Batterham, A.M., Bock, S., Robson, C., Stokes, K. (2006). Assessment of low-to-moderate intensity physical activity thermogenesis in young adults using

synchronized heart rate and accelerometry with branched-equation modeling. *Journal of Nutrition,* **136(4)**, 1037-1042.

Thompson, D.A., Wolfe, L.A., Eikelboom, R. (1988). Acute effects of exercise intensity on appetite in young men. *Medicine and Science in Sports and Exercise,* **20**, 222-227.

Tönjes, A., Scholz, M., Fasshauer, M., Kratzsch, J., Rassoul, F., Stumvoll, M., Blüher. M. (2007). Beneficial effects of a 4-week exercise program on plasma concentrations of adhesion molecules. *Diabetes Care*. **30(3)**.

Tremblay, A., Almeras, N., Boer, J., Kranenbarg, E.K., Despres, J.P. (1994). Diet composition and postexercise energy balance. *American Journal of Clinical Nutrition,* **59**, 975-979.

Tsetsonis, N.V., Hardman, A.E. (1996). Reduction in postprandial lipemia after walking: influence of exercise intensity. *Medicine and Science in Sports and Exercise*, **28(10)**, 1235-1242.

Tsofliou, F., Pitsiladis, Y.P., Malkova, D., Wallace, A.M., Lean, M.E.J. (2003). Moderate physical activity permits acute coupling between serum leptin and appetite-satiety measures in obese women. *International Journal of Obesity,* **27**, 1332-1339.

Tuomilehto, J., Lindström, J., Eriksson, J.G., Valle, T.T., Hämäläinen, H., Ilanne-Parikka, P., Keinänen-Kiukaanniemi, S., Laakso, M., Louheranta, A., Rastas, M., Salminen, V., Uusitupa, M. Finnish Diabetes Prevention Study Group. (2001). Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine*, **344(18)**, 1343-1350.

Turner, J.E., Markovitch, D., Betts, J.A., Thompson, D. (2010). Nonprescribed physical activity energy expenditure is maintained with structured exercise and implicates a compensatory increase in energy intake. *American Journal of Clinical Nutrition*, **in press**

Turcotte, L.P., Fisher, J.S. (2008). Skeletal muscle insulin resistance: roles of fatty acid metabolism and exercise. *Physical Therapy*, **88(11)**, 1279-1296.

Ueda, S.Y., Yoshikawa, T., Katsura, Y., Usui, T., Fujimoto, S. (2009). Comparable effects of moderate intensity exercise on changes in anorectic gut hormone levels and energy intake to high intensity exercise. *Journal of Endocrinology*, **203(3)**, 357-364.

Ueda, S.Y., Yoshikawa, T., Katsura, Y., Usui, T., Nakao, H., Fujimoto, S. (2009). Changes in gut hormone levels and negative energy balance during aerobic exercise in obese young males. *Journal of Endocrinology*, **201(1)**, 151-159.

Utter, A.C., Nieman, D.C., Ward, A.N., Butterworth, D.E. (1999). Use of the leg-to-leg bioelectrical impedance method in assessing body-composition change in obese women. *American Journal of Clinical Nutrition*. **69**, 603-607.

US Department of Health and Human Services. (1996). Physical activity and health: a report of the Surgeon General. Atlanta: US Department of Health and Human Services.

Van der Kooy, K., Seidell, J.C. (1993). Techniques for the measurement of visceral fat: a practical guide. *International Journal of Obesity and Related Metabolic Disorders*, **17(4),** 187-196.

Van der Poll, T., Coyle, S.M., Barbosa, K., Braxton, C.C., Lowry, S.F. (1996). Epinephrine inhibits tumor necrosis factor-alpha and potentiates interleukin 10 production during human endotoxemia. *Journal of Clinical Investigation*, **97**, 713–719.

Van der Wal, A.C., Das, P.K., Tigges, A.J., Becker, A.E. (1992). Adhesion molecules on the endothelium and mononuclear cells in human atherosclerotic lesions. *American Journal of Pathology*, **141**, 1427–1433.

Van Etten, L.M.L.A., Westerterp, K.R., Verstappen, F.T.J., Boon, B.J.B., Saris, W.H.M. (1997). Effect of an 18-wk weight-training program on energy expenditure and physical activity. *Journal of Applied Physiology*, **82**, 298-304.

Van Oostrom, A.J.H.H.M., Rabelink, T.J., Verseyden, C., et al., (2004). Activation of leukocytes by postprandial lipemia in healthy volunteers. *Atherosclerosis*, **177**, 175-182.

Van Oostrom, A.J.H.H.M., Van Wijk, J.P.H., Cabezas, M.C. (2004). Lipaemia, inflammation and atherosclerosis: novel opportunities in the understanding and treatment of atherosclerosis. *Drugs*, **64(2)**, 19-41.

Verger, P., Lanteaume, M.T., Louis-Sylvestre, J. (1994). Free food choice after acute exercise in men. *Appetite*, **22(2),** 159-164.

Verger, P., Lanteaume, M.T., Louis-Sylvestre, J. (1992). Human intake and choice of foods at intervals after exercise. *Appetite*, **18(2)**, 93-99.

Vogel, R.A., Corretti, M.C., Plotnick, G.D. (1997). Effect of a single high-fat meal on endothelial function in healthy subjects. *American Journal of Cardiology*, **79**, 350-354.

Wadden, T.A., Anderson, D.A., Foster, G.D. (1999). Two-year changes in lipids and lipoproteins associated with the maintenance of 5% to10% reduction in initial weight: some findings and some questions. *Obesity Research*, **7**, 170–178.

Wallenius, V., Wallenius, K., Ahren, B., Rudling, M., Carlsten, H., Dickson, S.L., Ohlsson, C., Jansson, J.O. (2002). Interleukin-6-deficient mice develop mature-onset obesity. *National Medicine*, **8**, 75–79.

Walters, R.G., Jacquemont, S., Valsesia, A., de Smith, A.J., Martinet, D., Andersson, J., Falchi, M., Chen, F., Andrieux, J., Lobbens, S., Delobel, B., et al., (2010). A new highly penetrant form of obesity due to deletions on chromosome 16p11.2. *Nature*, **463(7281)**, 671-675.

Warburton, D.E., Nicol, C.W., Bredin, S.S. (2006). Health benefits of physical activity: the evidence. *CMAJ,* **174(6)**, 801-809.

Wareham, N. (2007). Physical activity and obesity prevention. *Obesity Reviews*, **8(1)**, 109-114.

Wasserman, D.H., Ayala, J.E. (2005). Interaction of physiological mechanisms in control of muscle glucose uptake. *Clinical and Experimental Pharmacology and Physiology*, **32**, 319–323.

Wearing, S.C., Hennig, E.M., Byrne, N.M., Steele, J.R., Hills, A.P. (2006). The biomechanics of restricted movement in adult obesity, *Obesity Reviews*, **7(1)**, 13-24.

Westerterp, K.R., Meijer, G.A.L., Janssenj, E.M.E., Saris, W.H.M., Ten Hoor, F. (1992). Long-term effect of physical activity on energy balance and body composition. *British Journal of Nutrition,* **68**, 21-30.

Westerterp, K.R., Goran, M.I. (1997). Relationship between physical activity related energy expenditure and body composition: a gender difference. *International Journal of Obesity and Related Metabolic Disorders*, **21(3)**, 184-188.

Westerterp, K.R., Speakman, J.R. (2008). Physical activity energy expenditure has not declined since the 1980s and matches energy expenditures of wild mammals. *International Journal of Obesity*, **32(8)**, 1256-1263.

Westerterp-Plantenga, M.S., Werwegen, C.R.T., Ijedema, M.J.W., Wijckmans, N.E.G., Saris, W.H.M. (1997). Acute effects of exercise or sauna on appetite in obese and nonobese men. *Physiology and Behaviour*, **62**, 1345-1354.

Whang, W., Manson, J.E., Hu, F.B., Chae, C.U., Rexrode, K.M., Willett, W.C., Stampfer, M.J., Albert, C.M. (2006). Physical exertion, exercise, and sudden cardiac death in women. *JAMA*, **295(12)**, 1399-1403.

Whybrow, S., Hughes, D.A., Ritz, P., Johnstone, A.M., Horgan, G.W., King, N., Blundell, J.E., Stubbs, R.J. (2008). The effect of an incremental increase in exercise on appetite, eating behaviour and energy balance in lean men and women feeding ad libitum. *British Journal of Nutrition*, **100(5)**, 1109-1115.

Wijga, A.H., Scholtens, S., Bemelmans, W.J., de Jongste, J.C., Kerkhof, M., Schipper, M., Sanders, E.A., Gerritsen, J., Brunekreef, B., Smit, H.A. (2010). Comorbidities of

obesity in school children: a cross-sectional study in the PIAMA birth cohort. *BMC Public Health*, **10**, 184.

Williams, P. T. (2001). Physical fitness and activity as separate heart disease risk factors: a meta-analysis. *Medicine and Science in Sports and Exercise*, **33**, 754–761.

Williamson, D.F. (1996). Dietary intake and physical activity as "predictors" of weight gain in observational, prospective studies of adults. *Nutrition Reviews*, **54(4)**, S101-109.

Wing, R.R. (1992). Behavioral treatment of severe obesity. *American Journal of Clinical Nutrition*, **55(2)**, 545S-551S.

Wojtaszewski, J.F., Richter, E.A. (2006). Effects of acute exercise and training on insulin action and sensitivity: focus on molecular mechanisms in muscle. *Essays Biochemistry*, **42**, 31-46.

Wojtaszewski, J.F., Jorgensen, S.B., Frosig, C., Mac Donald, C., Birk, J.B., Richter, E.A. (2003). Insulin signalling: effects of prior exercise. *Acta Physiologica Scandinavica*, **178**, 321-328.

Woo, R., Garrow, J.S., Pi-Sunyer, F.X. (1982). Effect of exercise on spontaneous calorie intake in obesity. *American Journal of Clinical Nutrition*, **36(3)**, 470-477.

Woo, R., Garrow, J.S., Pi-Sunyer, F.X. (1982). Voluntary food intake during prolonged exercise in obese women. *American Journal of Clinical Nutrition*, **36(3)**, 478-484.

Woo, R., Pi-Sunyer, F.X. (1985). Effect of increased physical activity on voluntary intake in lean women. *Metabolism*, **34(9)**, 836-841.

Wood, P.D., Stefanick, M.L., Williams, P.T., Haskell, W.L. (1991). The effects on plasma lipoproteins of a prudent weight reducing diet, with or without exercise, in overweight men and women. *New England Journal of Medicine*, **325**, 461-466.

Wright, D.C., Geiger, P.C., Han, D.H., Holloszy, J.O. (2006). Are tyrosine kinases involved in mediating contraction-stimulated muscle glucose transport? *American Journal of Physiology Endocrinology and Metabolism*, **290(1)**, E123-E128.

Wynne, K., Stanley, S., McGowan, B., Bloom, S. (2005). Appetite Control. *Journal of Endocrinology*, **184**, 291-318.

Xiang, G.D., Wang, Y,L. (2004). Regular aerobic exercise training improves endothelium-dependent arterial dilation in patients with impaired fasting glucose. *Diabetes Care*, **27(3)**, 801-802.

Zhang, J.Q., Thomas, T.R., Ball, S.D. (1998). Effect of exercise timing on postprandial lipemia and HDL cholesterol subfractions. *Journal of Applied Physiology*, **85(4)**, 1516-1522.

Zhang, J.Q., Nunez, G., Feathers, S., Hart, C.L., Yao, W.X. (2004). Effect of exercise timing on postprandial lipemia in hypertriglyceridemic men. *Canadian Journal of Applied Physiology*, **29(5)**, 590-603.

Zierath, J.R. (2002). Invited review: Exercise training induced changes in insulin signaling in skeletal muscle. *Journal of Applied Physiology*, **93**, 773-781.

Zilversmit, D.B. (1995). Atherogenic nature of triglycerides, postprandial lipidemia, and triglyceride-rich remnant lipoproteins. *Clinical Chemistry*, **41(1)**, 153-158.

Zunft, H., Friebe, D., Seppelt, B., et al., (1999). Perceived benefits and barriers to physical activity in a nationally representative sample in European Union. *Public Health Nutrition*, **2**, 153–160.

APPENDICES

Appendix Ia,b

WOULD YOU LIKE TO KNOW HOW FIT YOU ARE AND HOW YOUR APPETITE RESPONDS TO EXERCISE?

We are looking for female volunteers to participate in a research study investigating the effects of exercise on appetite biomarkers

If you are:

- a woman aged between 18 and 45 years
- heavier than you would like to be
- healthy but not a regular exerciser
- a non-smoker
- and you are keen to cycle

* (all food will be provided for 4 days)

Then you might like to take part in our study

If you think that you might be interested or would like more information, without any obligation to participate, please contact either:

- Eirini Manthou **Tel.:** 0141 201 0486, **E-mail :** eirinimanthou@yahoo.gr

or

- Dr Dalia Malkova **Tel.:**0141 201 0648, **E-mail:** dm88n@clinmed.gla.ac.uk

Or check: **www.fitnessfriendz.blogspot.com**

WOULD YOU LIKE TO BECOME MORE PHYSICALLY ACTIVE?

We are looking for female volunteers to participate in a research study investigating the effects of two different types of exercise programme on changes in body weight and other health-related outcomes.

If you are:

- a woman aged between 18 and 45 years
- heavier than you would like to be
- healthy but not a regular exerciser
- a non-smoker
- and would like to increase your level of physical activity, with a personalised 8-week programme in a supervised and supportive environment

Then you might like to take part in our study

If you think that you might be interested or would like more information, without any obligation to participate, then please contact either:

- Eirini Manthou **Tel.:** 0141 201 0486, **E-mail :** eirinimanthou@yahoo.gr

or

- Dr Dalia Malkova **Tel. :** 0141 201 0648, **E- mail:** dm88n@clinmed.gla.ac.uk

Or check: **www.freewebs.com/eirinimanthou**

Appendix IIa,b

VOLUNTEER INFORMATION SHEET

(Version 1, 2 August 2007)

Project Title: Energy balance control in response to a single exercise session

(Lay title: Energy balance and exercise**)**

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

What is the purpose of the study?

Our purpose is to investigate how exercise modifies the response of various hormones and other factors in the blood which affect appetite and metabolism after meal consumption. The results will help us to understand more about how exercise helps people to maintain a healthy body weight.

Why have I been chosen?

You have been chosen because you are a healthy adult woman aged between 18-45 years who is somewhat heavier than the ideal weight for your height.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?

1) In the first instance will be asked to meet us for a screening visit in which we will:

- discuss with you and complete confidential questionnaires regarding your health, diet and physical activity patterns to ensure that it is perfectly safe for you to participate in this study
- measure your blood pressure, height and weight to enable us to determine whether you fall into the group of people we wish to study
- give you digital scales and diet diaries and instructions on how to use them
- provide an opportunity for you to ask questions

2) We will then ask you to undertake a number of preliminary tests consisting of fitness test, body composition measurements and dietary assessment. These will include:

- **Fitness Test.** This test will be performed on an exercise bike. The test will be of ~25 minutes duration and will consist of 5 stages of increasing intensity. During the test your heart rate will be measured using a monitor attached to your chest and we will collect samples of the air that you breathe out via a mouthpiece. This will enable us to determine your fitness level and calculate the intensity for your later exercise session. The test will not involve a maximal effort.

- **Body composition measurements.** This will involve measurements of height and body mass and body fatness by using Tanita body composition scales. Tanita scales send a very low, safe electrical current through the body, which meets resistance from fat tissue but passes freely through lean tissue and thus assess body composition from the level of resistance met. This is completely painless. We will also measure round your waist and hips.

- **Food diary.** You will be given digital kitchen scales and food diaries with written instructions and will be asked to keep records of all foods and drinks consumed for two days prior to your first trial. Two days before your next visit you will be asked to repeat this diet.

3) After the preliminary tests you will be ready to participate in 2 main experimental trials, on exercise and another control. Each of the trials will take place ***over two days*** and last for approximately 24 hours (including overnight sleep at home).

Day 1 – You will be asked to consume breakfast and lunch at home by using food provided by us in advance. You will be advised to eat as much as you want and bring the rest back. On the afternoon of Day 1

you will be asked to come to laboratory and either cycle at a moderate intensity for ~60-90 minutes (exercise trial) or rest quietly for the same duration (control trial). At the start and end of exercise and at the equivalent times during the control trial, samples of expired air and blood will be taken by a qualified and experienced person. You will also be asked to fill a short appetite questionnaire. Then you will be provided with buffet style dinner which will be composed of a variety of foods. We will ask you to consume food from this buffet according to your appetite. You will then have your overnight rest at home.

Day 2 – You will arrive in laboratory at ~8:00 h and stay with us for whole day (~until 6:00 pm). A qualified and experienced person will insert a cannula (a tiny sterile plastic tube) into a vein of your arm, which we will use to take blood. During the day you will be provided with buffet style breakfast, lunch and dinner. The buffets will be composed of a variety of food that you can consume to appetite. Personal preferences will be taken into consideration. Samples of expired air and blood will be taken before and after each meal and every 30-60 minutes between meals. Following each blood sample you will be asked to fill in a short appetite questionnaire.

What else do I have to do?

Other than the specific tasks described above, we ask you to maintain your usual lifestyle but for two days prior to each trial refrain from alcohol, caffeine and exercise and keep dietary diaries which you will be asked to replicate before the next trial.

What are the possible disadvantages and risks of taking part?

- Fitness testing will not be at a maximal level but the possibility exists that, very occasionally, certain changes may occur during or shortly after the tests. They include abnormal blood pressure, fainting or a change in the normal rhythm of the heart beat.
- Blood sampling via the cannula may cause minor bruising, an inflammation of the vein or haematoma (a small accumulation of blood under the skin). Good practice, however, minimises this risk. Some people may feel faint when they give blood.
- There is a small possibility that taking part in this study will reveal a health problem that you already have such as high blood pressure. If such a problem is revealed, we will inform your GP to ensure that you receive appropriate treatment.

What are the possible benefits of taking part?

There may be no benefits to you but as a result of taking part in this study you will receive information about your level of physical fitness and diet. The findings of this study will be published in scientific journals so that understanding about how exercise influence energy balance regulation in the fasted state and

after meal consumption. We will provide you with feedback about the main study findings and also about your own results and would be delighted to explain results and discuss the implications with you.

What if something goes wrong?
The chance of something going wrong is extremely small. All of the procedures involved in this study are low risk and our screening tests are designed to ensure that you will only participate if it is safe for you to do so. In the unlikely event that you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal University of Glasgow complaints mechanisms may be available to you.

Will my taking part in this study be kept confidential?
All information that is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the University will have your name and address removed so that you cannot be recognised from it.

What will happen to my samples after the study has finished?

The blood samples that you provide for this study may be useful for future research into the prevention and treatment of excess body weight gain and related conditions such as diabetes and heart disease; this may involve analysis of certain genes associated with these diseases. Any use of your samples for future research will require further approval from a Research Ethics Committee and samples will be analysed in such a way that the results will not be directly traceable to you. If you do not wish your samples to be used for future research, please indicate this on the consent form.

Who has reviewed the study?
This study has been reviewed and approved by the Faculty of Biomedical and Life Sciences Ethics committee at the University of Glasgow.

Contact for Further Information

Any questions about the procedures used in this study are encouraged. If you have any doubts or questions, please ask for further explanations by contacting Eirini Manthou, tel: 0141 201 0486, e- mail: e.manthou.1@research.gla.ac.uk or Dr Jason Gill, tel: 0141 3302916, e- mail: j.gill@bio.gla.ac.uk or Dr Dalia Malkova, tel: 0141 201 0648, e-mail: dm88n@clinmed.gla.ac.uk

You will be given a copy of this information sheet and a signed consent form to keep for your records.

VOLUNTEER INFORMATION SHEET

Project title: Impact of exercise programmes with similar energy expenditure and intensity but different frequency and duration on metabolic risk factors of chronic diseases and energy balance in overweight women.

Lay title: Effects of different exercise patterns on health and fitness

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

What is the purpose of the study?
Current physical activity guidelines recommend that all adults participate in at least 30 minutes of moderate-intensity physical activity on 5 days of the week. This equates to 150 minutes of physical activity per week. Some recent scientific data suggests that the performing exactly the same amount of exercise in a format where longer durations of exercise are performed on fewer days of the week might provide greater beneficial effects, but further study is needed to clarify this issue. This study will assess the effects of two different 8-week exercise programmes, both involving 150 minutes of moderate-intensity exercise per week, on outcomes related to health and fitness. In one programme, volunteers will perform 30 minutes of exercise on 5 days of each week and in the other programme, volunteers will perform 75 minutes of exercise on 2 days of each week. The results will help us to understand more about how exercise can improve health and help people to maintain a healthy body weight.

Why have I been chosen?
You have been chosen because you are a healthy adult woman aged between 18-45 years who is somewhat heavier than the ideal weight for your height.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?
1) In the first instance will be asked to attend for a screening visit in which we will:

- discuss with you and complete confidential questionnaires regarding your health, family history and physical activity to ensure that it is perfectly safe for you to participate in this study.
- measure your height, weight and blood pressure
- provide an opportunity for you to ask questions

After this visit you will be assigned to one of the two exercise groups.

2) We will then ask you to undertake a number of tests to determine your level of health and fitness. These will include:

- **Monitoring physical activity and diet** – we will ask you to weigh and record everything that you eat and drink for a week and to record all your activities during this period in a diary during the week before you start the exercise programme and during the final week of the exercise programme. We will also ask you to wear a heart rate monitor during this week and use this information calculate how many calories you burn during normal daily living. To enable us to do this calculation, we will need to measure your heart rate and collect the air you breathe out during a range of activities (such as lying, sitting, standing and walking) in the laboratory. You should allow about 0.5 hours to complete these laboratory tests.
- **Exercise tests** – These tests will be performed at the start of the programme, half way through the programme and at the end of the programme and will involve you cycling on an exercise bike at different speeds and we will monitor your heart rate and collect the air you breathe out to determine your fitness level. We will also take small blood samples during the test to determine the amount of lactic acid in your blood (this is what makes your legs burn when you exercise hard). Blood sampling will be no more painful than a simple blood test as samples will be obtained from a tiny plastic tube called a ‘cannula’ placed in a forearm vein. The tests will not involve a maximal effort and will each last about 30 to 40 minutes.
- **Assessment of body composition –** we will measure your weight and height and measure around your waist and your hips. We will also use callipers to measure skin fold thickness at four different sites (a sophisticated version of "pinch an inch") or by a method called

bioimpedance, a painless method which determines the amount of fat you are carrying from the electrical conductivity of your body. These measurements only take a few minutes and can be made on the same day as other tests at the start and at the end of the exercise programme.

- **Measurement of Resting Metabolic Rate** – This test will be performed before the start of the exercise programme and also one and three days after you complete the final session of the exercise programme. The test will involve you coming into the lab after an overnight fast and lying comfortably on a couch for about 25 minutes with a clear canopy (like a large spaceman's helmet) over your head. Most people find this quite relaxing. The air that you breathe out will be monitored and from this the number of calories and the amount of fat and carbohydrate that your body is burning will be assessed. After this, a small blood sample will be taken from a vein in your arm to measure factors which influence risk of heart disease and diabetes such as blood sugar and fat levels, and various hormones such as insulin which controls blood sugar levels.

3) You will then undertake the 8-week exercise programme which will be differing according to the group you have been allocated to:

- **Group 1** will of cycle on an exercise bike for 75-minutes on two days per week, with each session in the format of 37.5 minutes, followed by a 15-30 minute break, followed by another 37.5 minutes.
- **Group 2** will cycle on an exercise bike for 30-minutes on five days per week.

The intensity of the exercise sessions will be individually tailored and will increase progressively throughout the 8-week programme. All exercise sessions will be supervised and will take place in either the exercise laboratories in the Institute of Biomedical and Life Science or in Yorkhill Hospital (at your convenience).

4) At the end of the exercise programme the tests undertaken at the start of the programme (i.e, exercise tests, assessment of body composition, measurement of resting metabolic rate) will be repeated to determine the effect of the exercise programme on these factors.

What else do I have to do?
Other than the specific tasks described above, we ask you to maintain your usual lifestyle.

What are the possible disadvantages and risks of taking part?

- Exercise testing will not be at a maximal level but the possibility exists that, very occasionally, certain changes may occur during or shortly after the tests.

They include abnormal blood pressure, fainting or a change in the normal rhythm of the heartbeat.

- Blood sampling via the cannula may cause minor bruising, an inflammation of the vein or haematoma (a small accumulation of blood under the skin). Good practice, however, minimises this risk. Some people may feel faint when they give blood.
- There is a small possibility that taking part in this study will reveal a health problem that you already have such as high blood pressure. If such a problem is revealed, we will inform your GP to ensure that you receive appropriate treatment.

What are the possible benefits of taking part?

There may be no benefits to you but as a result of taking part in this study you will receive information about your level of heath and fitness and the opportunity to participate in a controlled, supervised exercise programme. The findings of this study will be published in scientific journals so that understanding about how exercise can help people to maintain a healthy body weight can be increased. This information may help make up better exercise guidelines.

We will provide you with feedback about the main study findings and also about your own results and would be delighted to explain results and discuss the implications with you.

What if something goes wrong?

The chance of something going wrong is extremely small. All of the procedures involved in this study are low risk and our screening tests are designed to ensure that you will only participate if it is safe for you to do so. In the unlikely event that you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal University of Glasgow complaints mechanisms may be available to you.

Will my taking part in this study be kept confidential?

All information that is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the University will have your name and address removed so that you cannot be recognised from it.

What will happen to my samples after the study has finished?

The blood samples that you provide for this study may be useful for future research into the prevention and treatment of excess body weight gain and related conditions such as diabetes and heart disease; this may involve analysis of certain genes associated with these diseases. Any use of your samples for future research will require further approval from a Research Ethics Committee and samples will be analysed in such a way that the results will not be directly

traceable to you. If you do not wish your samples to be used for future research, please indicate this on the consent form.

Who has reviewed the study?
This study has been reviewed and approved by the Institute of Biomedical and Life Sciences Ethics committee at the University of Glasgow.

Contact for Further Information

Any questions about the procedures used in this study are encouraged. If you have any doubts or questions, please ask for further explanations by contacting Eirini Manthou, tel: 0141 201 0486, e- mail: e.manthou.1@research.gla.ac.uk or Dr Jason Gill, tel: 0141 3302916, e- mail: j.gill@bio.gla.ac.uk or Dr Dalia Malkova, tel: 0141 201 0648, e-mail: dm88n@clinmed.gla.ac.uk

You will be given a copy of this information sheet and a signed consent form to keep for your records.

Appendix IIIa,b

Centre Number:
Study Number:
Subject Identification Number for this trial:

CONSENT FORM

Title of Project: Energy balance control in response to a single exercise session

Name of Researchers: Eirini Manthou, Dr Dalia Malkova and Dr Jason Gill

Please initial box

1. I confirm that I have read and understand the information sheet (Version 1, 2 August 2007) for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected. ☐
3. I agree to take part in the above study. ☐

_____	_____	_____
Name of subject	Date	Signature
_____	_____	_____
Name of Person taking consent (if different from researcher)	Date	Signature
_____	_____	_____
Researcher	Date	Signature

1 for subject; 1 for researcher

Centre Number:
Study Number:
Subject Identification Number for this trial:

CONSENT FORM

Title of Project:

Impact of exercise programs with similar energy expenditure and intensity but different frequency and duration on metabolic risk factors of chronic diseases and energy balance in overweight women.

Name of Researcher: Eirini Manthou, Dr Dalia Malkova and Dr Jason Gill

Please initial box

1. I confirm that I have read and understand the information sheet dated …… for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected. ☐

3. I agree to take part in the above study. ☐

Name of subject	Date	Signature
Name of Person taking consent (if different from researcher)	Date	Signature
Researcher	Date	Signature

1 for subject; 1 for researcher

Appendix IV

HEALTH SCREEN FOR STUDY VOLUNTEERS

Name: …….

It is important that volunteers participating in research studies are currently in good health and have had no significant medical problems in the past. This is to ensure (i) their own continuing well-being and (ii) to avoid the possibility of individual health issues confounding study outcomes.

Please complete this brief questionnaire to confirm fitness to participate:

1. **At present**, do you have any health problem for which you are:
   - (a) on medication, prescribed or otherwise — yes [ ] no [ ]
   - (b) attending your general practitioner — yes [ ] no [ ]
   - (c) on a hospital waiting list — yes [ ] no [ ]
2. In the past two years**, have you had any illness which required you to:**
   - **(a) consult your GP — yes [ ] no [ ]**
   - **(b) attend a hospital outpatient department — yes [ ] no [ ]**
   - **(c) be admitted to hospital — yes [ ] no [ ]**
3. Have you **ever had any of the following:**
   - **(a) Convulsions/epilepsy — yes [ ] no [ ]**
   - **(b) Asthma — yes [ ] no [ ]**
   - **(c) Eczema — yes [ ] no [ ]**
   - **(d) Diabetes — yes [ ] no [ ]**
   - **(e) A blood disorder — yes [ ] no [ ]**
   - **(f) Head injury — yes [ ] no [ ]**
   - **(g) Digestive problems — yes [ ] no [ ]**
   - **(h) Hearing problems — yes [ ] no [ ]**
   - **(i) Problems with bones or joints — yes [ ] no [ ]**
   - **(j) Disturbance of balance/co-ordination — yes [ ] no [ ]**
   - **(k) Numbness in hands or feet — yes [ ] no [ ]**

(l) Disturbance of vision **yes [ ] no [ ]**

(m) Thyroid problems **yes [ ] no [ ]**

(n) Kidney or liver problems **yes [ ] no [ ]**

(o) Chest pain or heart problems **yes [ ] no [ ]**

(p) Any other health problems **yes [ ] no [ ]**

4. For female volunteers only

(a) Are you pregnant or think that you might be pregnant yes [ ] no [ ]

(b) Do you take the contraceptive pill or other hormone-based contraceptives

yes [ ] no [ ]

(c) Are you postmenopausal **yes [ ] no [ ]**

(d) Are you receiving Hormone Replacement Therapy (HRT) yes [ ] no [ ]

5. Have any of your immediate family **ever had any of the following: (if yes please give details including age of first diagnosis)**

(a) Any heart problems **yes [ ] no [ ]**
(b) Diabetes **yes [ ] no [ ]**
(c) Stroke **yes [ ] no [ ]**
(d) Any other family illnesses **yes [ ] no [ ]**

6. Do you currently smoke **yes [ ] no [ ]**
Have you ever smoked **yes [ ] no [ ]**

If so, for how long did you smoke and when did you stop? ……

5. How many units of alcohol do you typically drink in a week? ……..

If YES to any question, please describe briefly if you wish (e.g. to confirm whether problem was short-lived, insignificant or well controlled.) (Use a separate sheet if necessary)

……

……

Name and address of GP

……

……

Blood pressure measured at screening……..mm Hg

Appendix V

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (October 2002)

LONG LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ

Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation

Translation from English is encouraged to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ

International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information

More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective.* Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

   ☐ Yes

   ☐ No → ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

   _____ **days per week**

   ☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

   _____ **hours per day**
   _____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

   _____ **days per week**

   ☐ No moderate job-related physical activity → ***Skip to question 6***

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

☐ No job-related walking → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day**
_____ **minutes per day**

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

☐ No traveling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**
_____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ **hours per day**
_____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days **walking** from place to place?

_____ **hours per day**
_____ **minutes per day**

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

_____ **days per week**

☐ No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

_____ **days per week**

☐ No moderate activity in garden or yard → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

☐ No moderate activity inside home → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**
_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**
_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

☐ No vigorous activity in leisure time → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**
_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

_____ **days per week**

☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?
_____ **hours per day**
_____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

_____ **hours per day**
_____ **minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

_____ **hours per day**
_____ **minutes per day**

This is the end of the questionnaire, thank you for participating.

Appendix VI

APPETITE QUESTIONNAIRE

Name: _____ Date: ____/____ /____ Trial: _____

Please answer the following questions by placing a vertical mark through the line for each question. Regard the end of each line as indicating the most extreme sensation you have ever felt and mark how you feel **NOW.**

Example

This is how to mark this line.

e.g. How happy are you (now)?

Not at all happy _____ As happy as I have ever been

Time: _____

1. How **hungry** do you feel (now)?

I am not hungry at all _____ **I have never been more hungry**

2. How **satisfied** do you feel (now)?

I am completely empty _____ **I cannot eat another bite**

3. How **full** do you feel (now)?

Not at all full _____ **Totally full**

4. How **much** do you think you **can eat** (now)?

Nothing at all _____ **A lot**

5. How strong is your **desire to eat** (now)?

Not at all strong _____ **Very strong**

Appendix VII

FOOD INVENTORY INSTRUCTIONS

It is important that you weigh and record everything that you eat and drink for the **two** days prior to each oral fat tolerance test (OFTT). Please do not take any alcohol on these days. Your last food and drink should be taken 12 hours before your OFTT appointment.

Please (i) start a separate page for each day.
(ii) start a separate line for each item.

Column 1
Record meal and time and place of eating.

Column 2
Describe each item as accurately as possible, stating where relevant:
(i) type and brand
(ii) whether food is fresh, dried, canned, frozen, salted, smoked, etc.
(iii) whether food is cooked, if so give method of cooking e.g. fried, baked, etc.

Column 3
Record the weight of each item after cooking:
(i) place scales on a level surface
(ii) place plate or container on top of scales
(iii) press 'ON/Reset' button to turn on scales
(iv) once zero appears, add first item of food
(v) record weight displayed
(vi) press reset button before weighing next item
Wherever possible, record weights in grams. If this is not possible, record weights in household measures (e.g. sugar or jam in teaspoons, stating whether level, rounded, or heaped).

Column 4
Record the weight of any leftovers, such as food remaining on plate, weight of container in which food has been weighed, apple cores, etc.

Columns 5 and 6
Please leave blank.

If food consists of several items, please list each on a separate line i.e. instead of writing 'one cheese sandwich', record separately the weights of bread margarine, cheese, etc.

Please remember to record all drinks, as well as food, giving weights where possible, or volumes if these are known. Record separately the weights of added milk and sugar.

An example is shown overleaf.

Food Inventory - Example

Name_____ **Date** _____

1. Time/Place	2. Description of food/drink	3. Weight of food/drink (g)	4. Weight of container/ leftovers (g)	Leave Blank	
Breakfast	Cornflakes (Kelloggs)	28			
8:30am	Milk (Sainsbury's virtually fat-free)	48			
Home	Bread (Mothers Pride, large white	76			
	sliced, toasted)				
	Flora margarine	7			
	Robinsons lemon marmalade	12			
	Coffee (instant)	2			
	Milk (whole pasteurised)	10			
Lunch	Cheese (Cheddar)	55			
1:00pm	Bread (white, crusty)	76			
Pub	Butter	4			
	Chutney (2 teaspoons)				
Snack	Coffee (instant)	2			
3:30pm	Coffee-mate	6			
Office	Mars Bar	35			
	Apple	76	8 (core)		
Dinner	Turkey Fillet (frozen, grilled)	102			
6:30pm	Potatoes, old, boiled	320	74		
Home			(leftover)		
	Peas (Birds Eye, frozen, boiled)	50			
	Heinz tomato ketchup	14			
	Yoghurt (Ski strawberry thick and	162	10		
	creamy)		(carton)		
	Coffee, filter	148			
	Milk (Sainsbury's virtually fat-free)	8			
Snack	Banana	107			
7:45pm	Orange Tango (can)	330			
Home					

Appendix VIII

Physical activity Diary

Name:

Date:

Instructions

- Try to be punctual with the time you start and finish an activity.
- Do not forget to write down the time you go to sleep, the time you wake up and the time you wear your heart rate monitor.
- Your data then will be collected and matched with your heart rate.

Time	Sleeping	Sitting	Standing	Walking	Self care	Driving	Exercise	Other activities
e.g. 23:00-7:00	√							
7:15								Put on monitor
7:00-8:50					√			
8:50-9:30		10 min	30 min					
9:30-9:40				√				Walk to work
9:40-13:20		2h	30 min					Work/office
13:20-14:10								Lunch
14:10-15:25		1 h		15 min				Work/office
15:25-15:50								Shopping
15:50-17:45		√						Work/office
17:45-17:55				√				Walk home
17:55-19:50								Home
19:50-20:10								Dinner
20:20-23:15		35 min	20 min					
23:15	√							Take off monitor