The influence of physical activity level on the sensitivity of the appetite control system

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The candidate confirms that the work submitted is her own, except where work which has formed part of jointly-authored publications has been included. The contribution of the candidate and the other authors to this work has been explicitly indicated below. The candidate confirms that appropriate credit has been given within the thesis where reference has been made to the work of others.

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Abstract

Background: Based on the non-linear relationship between energy intake and physical activity level demonstrated by Mayer et al. (1956), it has been proposed that there is a dysregulation of appetite at lower levels of physical activity leading to overconsumption, whereas at higher levels of physical activity, appetite control is more sensitive. However, the mechanisms underlying this relationship are not well understood.

Objective: This thesis aimed to shed light on the impact of habitual physical activity level in lean individuals and exercise training in individuals with overweight and obesity on homeostatic (physiological) and non-homeostatic (hedonic and eating behaviour traits) appetite processes, including those that initiate and terminate feeding (satiation) and suppress inter-meal hunger (satiety), as well as passive overconsumption (unintentional increase in energy intake with high-energy-density/high-fat foods).

Methods: A systematic review was conducted, followed by four experimental studies. The studies employed a multi-level experimental platform that included biological, behavioural and psychological aspects of energy balance including free-living physical activity, food intake, diet composition, food reward (liking and wanting), body composition, energy expenditure and fasting appetite-related peptides.

Results: The systematic review revealed a J-shaped relationship between physical activity level and energy intake, corroborating previous findings. Data from the experimental studies indicated that in lean individuals, physical activity did not influence satiation at meals varying in dietary fat content, but moderate to high active individuals showed enhanced satiety with better ability to adjust intake following preloads varying in energy content. Exercise training (12 weeks) in inactive individuals with overweight and obesity improved both homeostatic and non-homeostatic appetite control, which may be mediated by exercise-induced fat loss. Across all studies, physical activity was associated with lower body fat and greater daily energy expenditure, and energy density was positively associated with energy intake and passive overconsumption.

Conclusions: This thesis provides confirmatory evidence that physical activity impacts appetite control through a dual-process action expressed through an increased drive to eat from greater energy expenditure, together with enhanced satiety response to food in both lean and overweight/obese individuals. These processes may allow for more accurate matching of energy intake to requirements and a reduction in the risk of overconsumption at higher levels of physical activity.

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List of abbreviations

AG – Acylated ghrelin

AUC – Area under the curve

BES – Binge Eating Scale

BMI – Body mass index

CCK – Cholecystokinin

CoEQ – Control of Eating Questionnaire

COMPX – Compensation index

FFQ – Food frequency questionnaire

GLP-1 – Glucagon-like peptide-1

HE – High-energy

HEP – High-energy preload

HCHO – High-carbohydrate

HFAT – High-fat

HiPA – High physical activity level

HiMVPA – High level of moderate-to-vigorous physical activity

HOMA – Homeostasis model of risk assessment

HR – Heart rate

LE – Low-energy

LEP – Low-energy preload

LFPQ – Leeds Food Preference Questionnaire

LoPA – Low physical activity level

LoMVPA – Low level of moderate-to-vigorous physical activity

MET – Metabolic equivalent of a task

ModMVPA – Moderate level of moderate-to-vigorous physical activity

MVPA – Moderate-to-vigorous physical activity

NEAT – Non-exercise activity

NEP – No energy preload

NR – Not reported

PAEE – Physical activity energy expenditure

PFC – Prospective food consumption

PO – Passive overconsumption

PP – Pancreatic polypeptide

PYY – Peptide tyrosine tyrosine

RMR – Resting metabolic rate

RER – Respiratory exchange ratio

SED – Sedentary behaviour

SQ – Satiety quotient

SWA – SenseWear Armband

TEF – Thermic effect of food

TDEE – Total daily energy expenditure

TFEQ – Three Factor Eating Questionnaire

TG – Total ghrelin

VAS – Visual analogue scale

VO_{2max} – Maximal aerobic capacity/cardiorespiratory fitness

WC – Waist circumference

Chapter 1 – General introduction and background

The importance of physical activity in reducing morbidity and all-cause mortality (Blair, Cheng, & Holder, 2001; Booth, Roberts, Thyfault, Ruegsegger, & Toedebusch, 2017) and in weight management (Donnelly et al., 2009; Shaw, Gennat, O'Rourke, & Del Mar, 2006) has become increasingly evident. Despite the advances and efforts to help individuals become more active (e.g. fitness trackers, treadmill desks, active video games), most people still do not meet the recommendations of 150 minutes of moderate-to-vigorous physical activity per week established by the World Health Organisation (WHO; World Health Organization, 2017). Accelerometry data from four European countries reveal that less than 30% of adults achieve the WHO physical activity guidelines (Loyen et al., 2017). Physical inactivity is an important contributor to weight gain and obesity, despite claims suggesting that an unhealthy diet is mainly to blame (Malhotra, Noakes, & Phinney, 2015). However, the contribution of diet to obesity cannot be ignored. The current obesogenic food environment encourages intake of large portions and processed foods high in sugar, fat and energy density, which promote food consumption in excess of energy requirements (Swinburn et al., 2011). While obesity can be attributed to several factors other than physical inactivity and a nutrient-poor and energy-dense diet (UK Goverment's Foresight Programme, 2007), these are two key modifiable risk factors impacting on energy balance.

1.1 Defining energy balance and appetite control

Energy balance and resulting effects on body weight are the product of a complex relationship between energy intake and energy expenditure. Energy intake is modulated by the appetite control system through food consumption and eating behaviour. Energy intake is largely influenced by a combination of internal biological factors such as resting metabolic rate (RMR; Caudwell, Finlayson, et al., 2013) and appetite-related peptides (Huda, Wilding, & Pinkney, 2006; Murphy & Bloom, 2004), as well as external nutritional factors such as the energy density of the food consumed (Stubbs, Harden, Murgatroyd, & Prentice, 1995), with intake being greater at higher levels of RMR and energy density. Of the dietary macronutrients, fat has the strongest influence on energy density (9 kcal/g) compared to carbohydrate and protein (~4 kcal/g). Because of its higher energy density, fat has been shown to be less satiating per unit of energy than the other macronutrients, resulting in greater energy intake when consumed ad libitum, which has led to the term “passive overconsumption” (Blundell & MacDiarmid, 1997). Passive overconsumption can be defined as the

unintentional increase in energy intake arising from a failure to appropriately adjust intake in response to energy density (Blundell & MacDiarmid, 1997).

Appetite is controlled by several processes that form a psychobiological system that signals hunger (drives feeding), satiation (terminates feeding) and satiety (post-meal suppression of hunger), which in turn determine food and energy intake (Blundell, 1991; Blundell, Rogers, & Hill, 1987). These processes are influenced by episodic and tonic signals. Episodic signals occur on a meal-to-meal basis and diurnal variations in these signals reflect the size, pattern and frequency of meals and eating episodes. Episodic signals are primarily inhibitory (although they can be excitatory) and are related to meal initiation, termination and satiety. Tonic signals stem from body tissues and cellular metabolism, and convey information relating to energy availability and energy needs to the central nervous system (Morton, Cummings, Baskin, Barsh, & Schwartz, 2006). These homeostatic mechanisms interact with non-homeostatic processes, such as food hedonics, in the overall expression of appetite (Blundell & Finlayson, 2004). The complex relationships between homeostatic and non-homeostatic inputs, coupled with the current obesogenic food environment, can make individuals vulnerable to overconsumption and weight gain.

On the other side of the energy balance equation is total daily energy expenditure (TDEE), which is composed of RMR, followed by physical activity energy expenditure (PAEE) and thermic effect of food (TEF; Hall et al., 2012). Physical activity encompasses structured exercise in addition to occupational, household, transportation and other activities of daily living, termed non-exercise activity thermogenesis (NEAT; Caspersen, Powell, & Christenson, 1985). These components are illustrated in Figure 1-1. The proportion of each can vary widely between and within individuals depending on levels of physical activity and daily exercise regime. Additionally, it is important to distinguish between sedentary behaviour and physical inactivity. Sedentary behaviour can be defined as “any waking behaviour characterized by an energy expenditure ≤1.5 metabolic equivalents (METs), while in a sitting, reclining or lying posture”, whereas physical inactivity is “an insufficient physical activity level to meet present physical activity recommendations” (Tremblay et al., 2017). This thesis focuses on habitual physical activity levels (including inactivity) rather than sedentary behaviour.

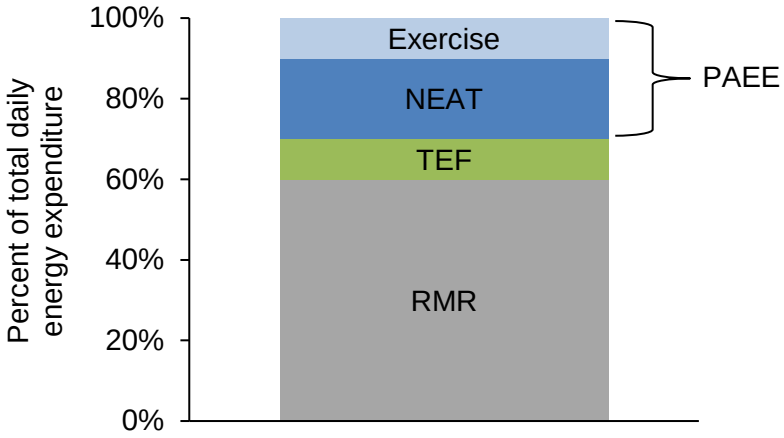

Figure 1-1 Components of total daily energy expenditure, which is composed primarily of RMR. Physical activity energy expenditure (PAEE) can be structured via exercise or non-exercise-based activities (NEAT) and the proportion can vary within and between individuals. The proportion of thermic effect of food (TEF) was generalised to ~10% TDEE. Adapted from Melanson (2017).

1.1.1 A note on physical activity, energy expenditure and body composition

Common beliefs regarding TDEE assume that it increases with physical activity in a dose-dependent manner, whereby greater physical activity levels lead to greater TDEE (Melanson, 2017). Recently, whether TDEE increases in proportion to physical activity level has been debated, and a constrained energy expenditure model has been proposed by Pontzer et al. (2016). These authors demonstrated that at lower levels of physical activity, TDEE increases linearly with physical activity, but at a certain threshold of much higher physical activity, TDEE plateaus. Thus, compensatory reductions in other metabolic processes or components of TDEE could occur with increasing physical activity to maintain energy expenditure within a certain narrow range (Pontzer et al., 2016). However, further evidence is required to validate this model, elucidate the mechanisms that could regulate TDEE and the specific components of TDEE affected at very high levels of physical activity.

It is also important to emphasise that within the general population, which is highly inactive and at the low end of the levels of physical activity (World Health Organization, 2017), an increase in physical activity will likely lead to an increase in TDEE and should remain a key component for weight loss and weight management (Donnelly et al., 2009; Shaw et al., 2006).

1.2 Psychobiological system of appetite control

The control of appetite can be conceptualised as a matrix of events and interactions occurring in three levels of the psychobiological system: psychological and behavioural events; peripheral physiology and metabolic events; and neurotransmitter and metabolic interactions in the brain (Blundell, 1991). The desynchronisation of these three levels occurs when appetite is disrupted, for example with eating disorders (and perhaps with physical inactivity). While this thesis will address some of the mechanisms involved in the peripheral level of the system such as gut and appetite-related peptides, it will mainly focus on the processes involved in the behavioural level of the system. This level incorporates the events and behaviours that lead to, arise during, terminate and occur after food consumption, and have been termed the Satiety Cascade (Blundell et al., 1987).

1.2.1 Satiety Cascade

As shown in Figure 1-2, hunger and hedonic sensations stimulate food intake, and prior to food consumption, the sight and smell of food generate gastrointestinal signals in anticipation of its ingestion as part of the cephalic phase of appetite. During and shortly after food consumption, negative feedback signals arise from the stomach and the small intestine to promote meal termination (satiation) and the post-meal suppression of hunger (satiety), which, in turn, coordinate meal size and frequency (Blundell, 1991). In the pre-absorptive phase of the Satiety Cascade, sensory inputs via chemoreceptors and mechanoreceptors, and humoral responses from gut peptides inform the brain on the amount and nutrient content of the ingested food (Blundell, 1991). The post-absorptive phase is characterised by the circulating metabolic satiety signals that arise from the digestion of nutrients and either reach the brain directly or are metabolised by peripheral tissues or organs, after which by-products may subsequently enter the brain (Blundell, 1991). As discussed below in Section 1.3, non-homeostatic (e.g. hedonic) factors also influence food intake and appetite control and should be acknowledged alongside homeostatic processes (Figure 1-2).

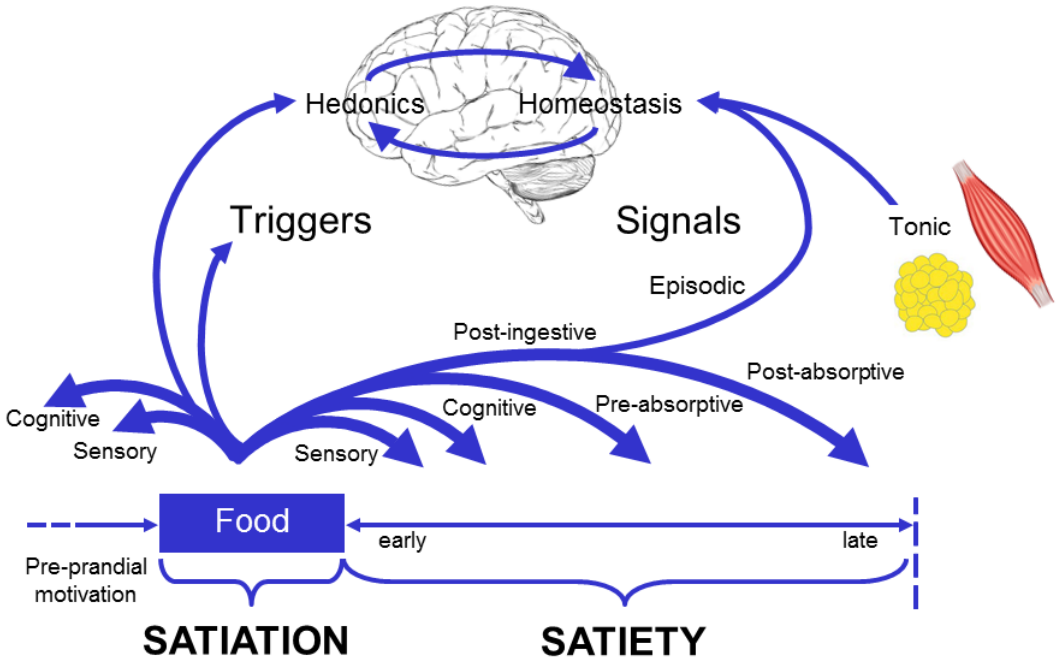

Figure 1-2 The Satiety Cascade highlighting the cross-talk between the hedonic and homeostatic appetite control systems. Adapted from Blundell and Finlayson (2008).

1.2.2 Gut and appetite-related peptides

On a meal-to-meal basis, following food intake and gastric emptying, the secretion of the orexigenic (appetite stimulating) peptide ghrelin is suppressed and a variety of anorectic (appetite inhibiting) peptides, such as cholecystokinin (CCK), glucagon-like peptide 1 (GLP-1), and peptide YY (PYY), among others, are released from the gut to promote the processes of satiation and satiety (Huda et al., 2006; Murphy & Bloom, 2004). In addition to episodic peptides, tonic signals such as leptin and insulin have also shown to influence appetite control and food intake (Schwartz, Woods, Porte, Seeley, & Baskin, 2000). A brief overview of the most commonly studied peptides, CCK, PYY, GLP-1, ghrelin, leptin and insulin, is provided here.

1.2.2.1 CCK

CCK is released from the small intestine shortly following food consumption and is involved in the process of satiation to reduce meal size and duration, and possibly in the early phases of satiety (de Graaf, Blom, Smeets, Stafleu, & Hendriks, 2004). The secretion of CCK increases in proportion to the dietary fat content of a meal (Feltrin et al., 2007; Pilichiewicz et al., 2006). However, it has been proposed that chronic high-fat intake attenuates the satiating properties of CCK, perhaps through a reduction in

the responsiveness of the vagal receptors, leading to greater food intake (Covasa, Grahn, & Ritter, 2000; French, Murray, Rumsey, Fadzlin, & Read, 1995).

1.2.2.2 PYY and GLP-1

PYY are GLP-1 are secreted from the same intestinal L-cells after food intake and have been proposed to be involved in satiety signalling to supress appetite following meal termination (de Graaf et al., 2004). PYY circulates mostly as its shortened form PYY_{3-36} and infusions of PYY_{3-36} decrease food intake in humans (Karra & Batterham, 2010). Concentrations of PYY increase in proportion to the energy content of a meal and are reduced during fasting (Batterham et al., 2006). As one of the incretin hormones, GLP-1 stimulates the release of insulin, but it has been proposed that insulin resistance with obesity may hamper the postprandial secretion of GLP-1 (Cummings & Overduin, 2007; Verdich et al., 2001). Fat intake has been shown to increase the release of PYY to a greater extent than carbohydrate (Feltrin et al., 2007; Pilichiewicz et al., 2006), and to a prolonged release of GLP-1 (Elliott et al., 1993). However, it appears the PYY response to dietary fat is attenuated in individuals with obesity compared to those with a healthy weight (Batterham et al., 2006).

1.2.2.3 Ghrelin

Ghrelin is mainly secreted from the stomach and exists in two forms: acylated and deacylated ghrelin (Kojima et al., 1999). It has been suggested that only the acylated form, which only accounts for 10-20% of circulating concentrations, can cross the blood-brain barrier and exert an effect on appetite (Kojima & Kangawa, 2005). Plasma concentrations increase before meals and decrease following food consumption, suggesting a role in stimulating hunger and eating behaviour, unlike other appetite-related peptides that provide negative feedback signals to promote satiety (Karra & Batterham, 2010). Ghrelin administration has been shown to increase hunger and food intake in humans (Wren et al., 2001). In addition to its episodic role, ghrelin may also be linked to tonic appetite control as a compensatory hormone to restore body weight status; with obesity, ghrelin concentrations appear to be lower, whereas with weight loss, they increase (Karra & Batterham, 2010).

1.2.2.4 Insulin and leptin

Considered as negative feedback signals released in proportion to body fat, leptin and insulin have been hypothesised to act directly in the central nervous system to reduce appetite and energy intake (Schwartz et al., 2000). Insulin, secreted from the pancreas, was the first hormone considered as an adiposity signal impacting on the control of appetite to supress hunger and food intake (Woods, Lotter, McKay, & Porte, 1979). This was followed by leptin, secreted from the adipocytes, whose discovery provided a direct link between the energy stores within adipose tissue and central appetite mechanisms (Campfield, Smith, Guisez, Devos, & Burn, 1995; Zhang et al., 1994). Very low circulating concentrations of leptin (or leptin deficiency) have been associated with marked hyperphagia and obesity (Farooqi & O'Rahilly, 2009), highlighting its role in inhibiting the drive to eat. Despite circulating concentrations of both leptin and insulin being strongly positively associated with the degree of adiposity (Bagdade, Bierman, & Porte, 1967; Considine et al., 1996), at higher levels of body fat as in the obese state, there appears to be a resistance to the direct action of leptin and insulin in the hypothalamus (Morton et al., 2006; Schwartz et al., 2000). This provides a rationale as to why individuals with obesity continue to eat and feel hungry despite having excessive amounts of body fat stores. Moreover, it is believed that an interaction between episodic and tonic peptides exists, with a reduced sensitivity to leptin or insulin leading to blunted signalling of satiety peptides such as CCK and GLP-1 (Cummings & Overduin, 2007; Flint et al., 2007; Morton et al., 2006). Indeed, the postprandial response of insulin has been associated with satiety in lean individuals, but less so in individuals with obesity (Flint et al., 2007; Flint et al., 2006; Holt, Brand Miller, & Petocz, 1996; Speechly & Buffenstein, 2000; Verdich et al., 2001).

1.3 Non-homeostatic factors involved in appetite control

In addition to the homeostatic mechanisms, non-homeostatic factors involved in appetite control include food hedonics (food palatability and reward) and eating behaviour traits (Berthoud, 2006; Mela, 2006). These traits characterise certain eating behaviours such as dietary restraint, disinhibition, (Stunkard & Messick, 1985), binge eating (Gormally, Black, Daston, & Rardin, 1982) and control over food cravings (Hill, Weaver, & Blundell, 1991), considered as risk factors in the susceptibility for overconsumption and weight gain (Blundell et al., 2005).

Hedonic thoughts about food and the sensory appreciation of certain food attributes like salt, sugar and fat determine food preference and choice, and thereby contribute to meal size and frequency (Dalton & Finlayson, 2013). Food hedonics reflect the separate processes of ‘liking’ and ‘wanting’ (Berridge & Robinson, 2003).

Liking can be defined as the degree of sensory pleasure obtained from foods, whereas wanting is the motivation or attraction towards certain foods (Finlayson & Dalton, 2012). While both processes are involved in the motivation to eat, they operate as distinct entities where an increase in wanting may not necessarily predict an increase in liking and vice versa (Finlayson, King, & Blundell, 2007). Liking and wanting can be expressed explicitly through hedonic feelings towards a specific food (e.g. I like this) and the intent or desire to eat a specific food (e.g. I want this), respectively. Wanting can also be expressed implicitly without conscious awareness (e.g. being drawn to one food over another without knowing why). Wanting may be more important for overconsumption and maintenance of obesity than liking, which tends to remain stable within an individual and does not appear to be influenced by obesity (Cox, Perry, Moore, Vallis, & Mela, 1999; Dalton & Finlayson, 2013; Mela, 2006).

In today's obesogenic environment, the availability of highly palatable and often energy-dense foods raises the importance of hedonic influences on the control of food intake that occur independently from and/or in opposition to the energy need or weight status of an individual (Dalton, Finlayson, Esdaile, & King, 2013). Indeed, there is growing evidence to support the considerable functional overlap between the homeostatic and hedonic mechanisms of appetite control (Berthoud, 2004; Blundell & Finlayson, 2004), which could be linked by GLP-1 (Blundell et al., 2017), ghrelin (Erlanson-Albertsson, 2010; Goldstone et al., 2014), insulin and/or leptin (Morton et al., 2006). Consequently, hedonic signals occurring when palatable and energy-dense foods are ingested can disrupt or override homeostatic satiety signals and lead to overconsumption (Erlanson-Albertsson, 2005). This may be mediated by an accumulation of body fat which has been proposed to weaken satiety signalling (Cummings & Overduin, 2007; Flint et al., 2007; Morton et al., 2006), perpetuating overeating in individuals with excess body fat and obesity. However, it is important to note that palatability of food per se may not lead to overconsumption but it is rather the high energy density associated with palatable foods rich in fat and sugar that is driving the increase in energy intake (Mela, 2006). For example, consumption of highly palatable artificially sweetened low-calorie foods may not lead to overconsumption over energy requirements.

1.4 The influence of body composition and energy expenditure on energy intake

While there is evidence for the negative feedback mechanisms involved in satiation and satiety based on the interaction between tonic adiposity and episodic gut signals, less is known on the factors that drive hunger and food intake. Whether energy

expenditure and physical activity are drivers of energy intake is not well understood (Blundell, Goodson, & Halford, 2001). The relationship between energy expenditure and energy intake in humans was examined over 60 years ago (Edholm et al., 1970; Edholm, Fletcher, Widdowson, & McCance, 1955; Mayer, Roy, & Mitra, 1956). Mayer et al. (1956) demonstrated a relationship between occupational physical activity and daily energy intake in Bengali jute mill workers whose daily occupations ranged from "sedentary" to "very heavy work" whereby those performing "very heavy work" consumed more than those performing "light work" (Mayer et al., 1956). In line with Mayer, Edholm et al. (1970) found a strong relationship between TDEE and daily energy intake in army cadets over three weeks. Despite providing initial evidence for physiological processes and behavioural activities impacting on appetite and providing a demand for food intake, this concept was left dormant for several decades.

The roles of body composition and energy expenditure in driving food intake have recently been re-examined (Blundell, Finlayson, Gibbons, Caudwell, & Hopkins, 2015; Dulloo, Jacquet, Miles-Chan, & Schutz, 2017). Fat-free mass has been found to be strongly and positively associated with energy intake in lean and overweight/obese individuals (Blundell et al., 2012a; Weise, Hohenadel, Krakoff, & Votruba, 2014), corroborating findings from earlier but less known studies (Cugini et al., 1998; Lissner et al., 1989). In contrast, the relationship between fat mass and energy intake was found to be negatively associated with hunger and energy intake in lean but less so in overweight and obese individuals (Blundell et al., 2012a; Cugini et al., 1999; Cugini et al., 1998; Lissner et al., 1989). This supports the proposition that adiposity signals inhibiting food intake are blunted with higher levels of body fat (Morton et al., 2006; Schwartz et al., 2000). In addition to fat-free mass, RMR has also been shown to predict energy intake (Caudwell, Finlayson, et al., 2013; McNeil et al., 2017), which led to the suggestion that RMR (largely determined by fat-free mass) exerts a tonic day-to-day signal for hunger and the drive to eat (Blundell et al., 2012b). It has recently been shown that the associations between fat-free mass and energy intake are mediated by RMR (Hopkins, Finlayson, et al., 2016) and TDEE (Piaggi, Thearle, Krakoff, & Votruba, 2015), suggesting that the associations between fat-free mass and energy intake reflect the energetic demands created by metabolically active tissue.

1.5 Energy intake and appetite control along the spectrum of physical activity

The contribution of physical activity (behaviour) per se towards the drive to eat is less apparent and remains to be elucidated. In comparison to RMR, physical activity makes up a smaller proportion of TDEE and is more variable; therefore, its impact on energy

intake may be smaller and harder to quantify. Prior reports did not find significant associations between physical activity and energy intake (Blundell & King, 1998) in addition to others showing that seven days of imposed inactivity did not lead to a reduction of energy intake (Stubbs, Hughes, Johnstone, Whybrow, et al., 2004). More recently, a systematic review (Donnelly et al., 2014) and a meta-analysis (Schubert, Desbrow, Sabapathy, & Leveritt, 2013) supported these with little evidence that physical activity or exercise, whether acute or chronic, leads to changes in energy intake. However, the acute or relatively short-term nature of these studies may not have been long enough to demonstrate a compensatory rise in energy intake with habitual physical activity (Stubbs, Sepp, Hughes, Johnstone, Horgan, et al., 2002; Stubbs, Sepp, Hughes, Johnstone, King, et al., 2002; Whybrow et al., 2008) and as originally demonstrated by Mayer et al. (1956). Indeed, a strong relationship was found between weekly objectively-measured habitual physical activity and weekly food intake (based on food diaries) in 300 middle-aged women (Tucker, 2016).

It is important to note that the study by Mayer et al. (1956) revealed a non-linear relationship between habitual physical activity level on energy intake. As shown in Figure 1-3, in the jute mill workers on the right side with higher levels of occupational physical activity (e.g. “medium” to “very heavy” work), daily energy expenditure and energy intake were closely matched, but on the left side at low levels of occupational physical activity this coupling was lost, such that daily energy intake exceeded expenditure in those performing “sedentary” to “light” work (Mayer et al., 1956). Additionally, those in the sedentary physical activity category were also heavier than those in the light to very heavy work categories (Mayer et al., 1956).

Based on the study by Mayer et al. (1956), it was proposed that appetite control is enhanced with increasing levels of physical activity (Blundell, 2011). In contrast, physical inactivity could not only reduce TDEE but also lead to appetite dysregulation, overconsumption and eventually weight gain (Blundell, 2011). Indeed, according to Jacobs (2006), “the late Henry L Taylor favoured a model that linked energy intake to energy expenditure in a J-shaped curve (personal communication, late 1970s). The first part of his concept was that energy intake is in exact homeostasis with energy expenditure under conditions of high energy expenditure. The second part was that there is a failure of homeostasis in a sedentary lifestyle because of its accompanying low energy expenditure. He postulated that body signals go awry in sedentary lifestyles; when a person does no physical work, the body will not recognize that it is being overfed. Sedentary persons may lose the innate ability to compensate for inactivity by reducing their eating” (p.189). Thus, Blundell (2011) amended the Mayer curve and suggested that individuals with low levels of physical activity could be considered as being within a “non-regulated zone” of appetite control (left side of Figure 1-3), whereas those with higher levels of physical activity could be

within a “regulated zone” of appetite control (right side of Figure 1-3). However, this model of physical activity and appetite control is based on limited evidence and the factors and mechanisms contributing to this proposed overconsumption at lower levels of physical activity and more sensitive appetite control at higher levels remain to be fully elucidated.

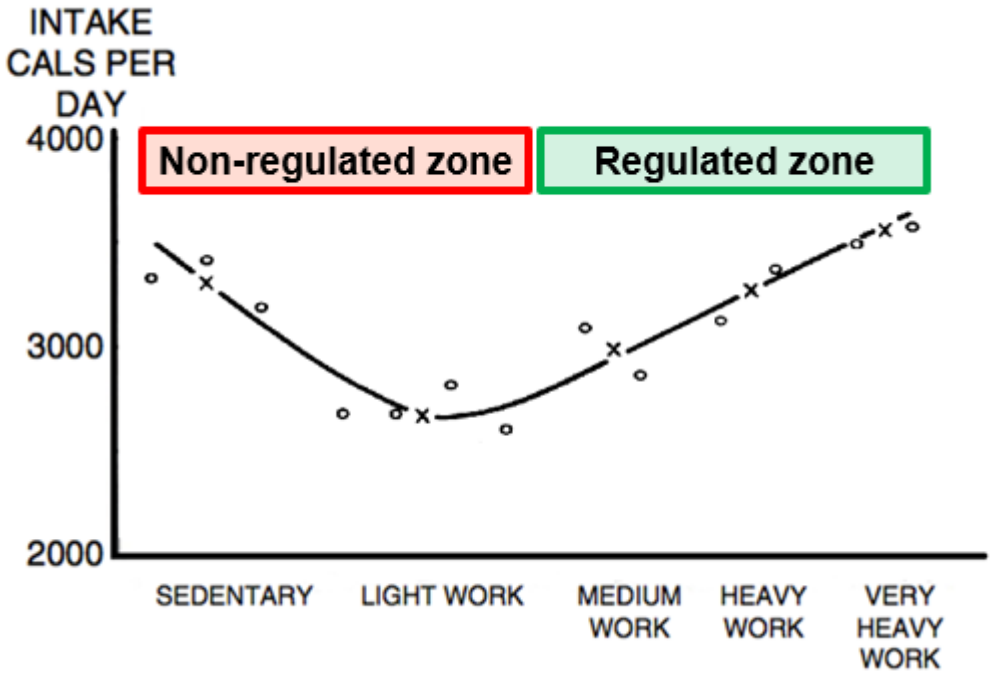

Figure 1-3 Relationship between occupational physical activity level and energy intake divided into non-regulated zone (high levels of sedentary behaviour and low levels of physical activity) and regulated zone of appetite control (medium to very high levels of physical activity) based on the study by Mayer et al. (1956). Adapted from Blundell (2011).

1.5.1 The impact of physical activity on the mechanisms of appetite control

There has been increasing interest on the influence of physical activity (and exercise) on the mechanisms of appetite control as it plays an integral (and readily modifiable) part in energy balance and the regulation of body weight (Blundell, Gibbons, Caudwell, Finlayson, & Hopkins, 2015; Martins, Morgan, & Truby, 2008; Stensel, 2010; Thackray, Deighton, King, & Stensel, 2016). Emerging studies are shedding light on the mechanisms contributing to the proposed dysregulation of appetite at lower levels of physical activity and more sensitive appetite control at higher levels of physical activity. Acutely, exercise has been shown to influence gastric emptying (Horner, Schubert, Desbrow, Byrne, & King, 2015), attenuate the release of ghrelin and increase the secretion of PYY, GLP-1 and pancreatic polypeptide (Broom, Batterham,

King, & Stensel, 2009; Broom, Stensel, Bishop, Burns, & Miyashita, 2007; Deighton, Barry, Connon, & Stensel, 2013; Douglas et al., 2017; Schubert, Sabapathy, Leveritt, & Desbrow, 2014), and increase feeding latency i.e. the timing when food in consumed (King, Wasse, & Stensel, 2013). Chronic exercise may increase the secretion of GLP-1 and PYY (Lund et al., 2013; Martins, Kulseng, King, Holst, & Blundell, 2010). Therefore, physical activity (and exercise) may interact with food intake to enhance hormonal satiety signalling (Stensel, 2010). Moreover, regular physical activity and exercise training are associated with several other physiological adaptations such as improved sensitivity to insulin (Goodyear & Kahn, 1998) and leptin (Dyck, 2005; Steinberg et al., 2004), substrate metabolism (Richter & Ruderman, 2009) and body composition (Shaw et al., 2006; Stiegler & Cunliffe, 2006), which have been proposed as mechanisms involved in food intake and eating behaviour (Figure 1-4; Blundell, Gibbons, et al., 2015). Evidence suggests that chronic exercise influences appetite control through a dual-process action which increases fasting hunger but also post-meal satiety (King et al., 2009). Therefore, inactive individuals in the non-regulated zone of appetite could have weakened satiety signalling or dysfunction of other appetite-related processes or traits, whereas active individuals in the regulated zone could have a more sensitive appetite control system in order for energy intake to be better matched to energy expenditure (Blundell, 2011).

While there is strong support that habitual physical activity affects homeostatic mechanisms controlling food intake, less is known on its effect on non-homeostatic processes such as food hedonics and eating behaviour traits, and their contribution to appetite control across the levels of physical activity. The potential influence of habitual physical inactivity on food hedonics and eating behaviour traits may contribute to the overconsumption seen in the non-regulated zone of appetite, but this remains unknown. In fact, few studies have focused on the differences in homeostatic and non-homeostatic appetite control between physically active and inactive individuals. These are systematically reviewed in the following chapter and addressed throughout this thesis.

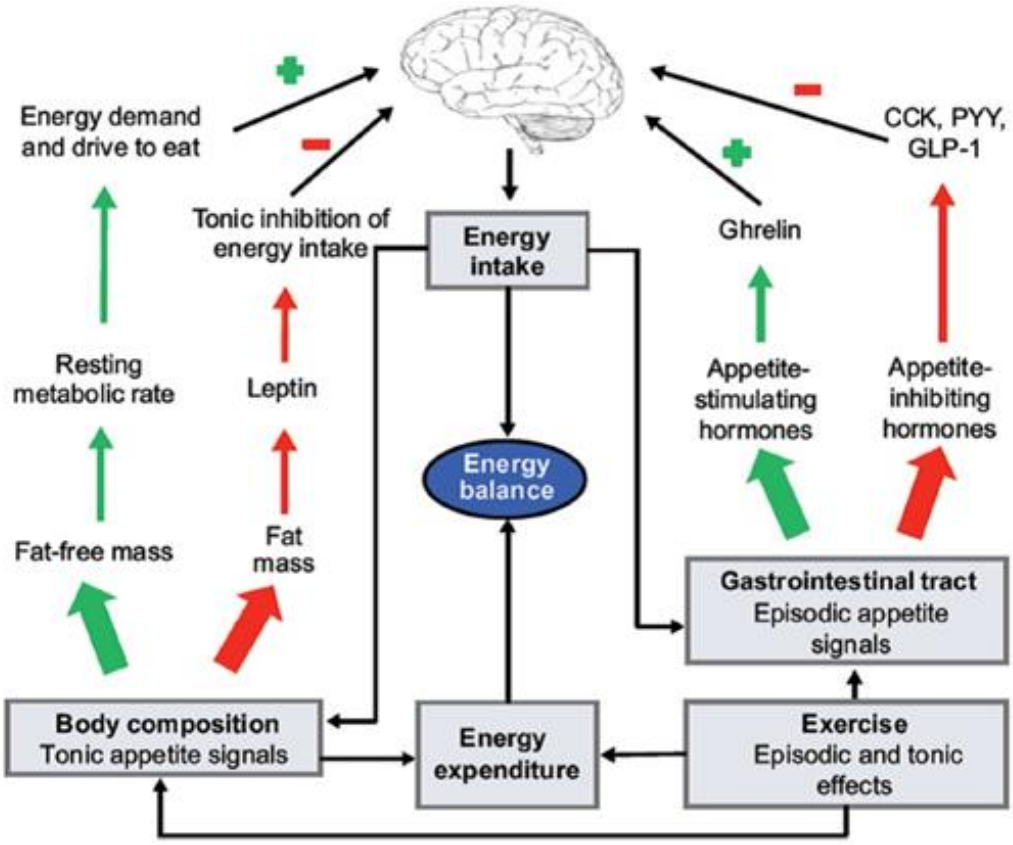

Figure 1-4 Model of the impact of exercise on the mechanisms of appetite control. Exercise increases fat-free mass, which through RMR increases the demand and drive to eat; reduces fat mass, which enhances the tonic inhibition of leptin on energy intake; and affects the release of episodic gut peptides to modulate hunger and satiety. From Blundell, Finlayson, et al. (2015).

1.5.2 Interaction between physical activity and diet composition on energy intake and energy balance

Whilst physical activity appears to affect several mechanisms of appetite control, whether it renders individuals less susceptible to overconsumption in the current obesogenic food environment has not been extensively examined. This is important to consider, with headlines stating “You cannot outrun a bad diet” (Malhotra et al., 2015). Only a few studies have investigated the impact of physical activity and diet composition on energy intake and energy balance. A study by Tremblay et al. (1994) in males found that consumption of a high-fat diet over two days following a 500-kcal exercise bout led to a positive energy balance, whereas consumption of a low-fat diet was able to maintain the energy deficit produced by exercise. Along those lines, Murgatroyd et al. (1999) showed in males that increasing the dietary fat content (and energy density) of an ad libitum diet in a day where exercise was imposed (~675 kcal) increased energy intake and led to a positive energy balance (albeit not statistically significant). Moreover, consumption of a high-fat diet while imposing inactivity resulted in a daily positive energy balance of approximately 1000 kcal more than with imposed exercise, and 1200 kcal more than with exercise on a low-fat diet. Other studies in males (King & Blundell, 1995) and females (King, Snell, Smith, & Blundell, 1996) corroborated these findings by demonstrating that the consumption of a high-fat meal following an exercise bout resulted in significantly greater relative energy intake (after considering the energy expenditure of the exercise) compared with a low-fat meal. Interestingly, palatability of both high-fat and low-fat meals increased after exercise compared to rest in females, but not in males (King et al., 1996). These studies highlight the potency and robustness of the phenomenon of passive overconsumption with a high-fat/energy-dense diet, regardless of the added energy expended through acute exercise. However, whether being physically active in general enhances the response to dietary manipulations is also of interest. This will be further addressed in the following chapter and throughout this thesis.

1.6 Overall thesis aims

The literature regarding the influence of habitual physical activity on the sensitivity of appetite control is limited. Whether physical activity enhances appetite control and by which mechanisms have yet to be fully resolved. This thesis aims to shed light on the impact of habitual physical activity level in non-obese individuals and exercise training in individuals with overweight and obesity on homeostatic and hedonic appetite processes; namely satiation, satiety and passive overconsumption. To achieve this, the experimental studies within this thesis employ a multi-level experimental platform that includes biological, behavioural and psychological aspects of energy balance.

1.6.1 Specific objectives

- Systematically review the literature examining appetite control in active and inactive individuals, and in response to exercise training in inactive individuals (Chapter 2).

- Investigate the effect of habitual physical activity level on satiation and the hedonic response to ad libitum meals varying in dietary fat content in non-obese individuals (Chapter 4).

- Investigate the effect of habitual physical activity level on satiety and the hedonic response to preloads differing in energy content in non-obese individuals (Chapter 5).

- Examine the associations among components of physical activity (including time spent in light, moderate and vigorous physical activity, energy expenditure and cardiorespiratory fitness), appetite control and energy intake in non-obese individuals (Chapter 6).

- Investigate the homeostatic and non-homeostatic responses to a 12-week exercise training intervention and to meals varying in dietary fat content in inactive overweight and obese individuals (Chapter 7).

- Examine the potential mechanisms underlying the impact of physical activity on appetite control including body composition, energy expenditure and non-homeostatic processes (all studies), and fasted appetite-related peptides (Chapters 4, 6 and 7).

Chapter 2 – Does habitual physical activity increase the sensitivity of the appetite control system? A systematic review

2.1 Introduction

Scientific studies have tended to examine the appetite responses to exercise rather than habitual physical activity levels per se, with few studies having specifically focused on the appetite control differences between physically active and inactive individuals. There is some evidence suggesting that habitual physical activity improves appetite control by enhancing satiety signalling (King et al., 2009; Long, Hart, & Morgan, 2002). Two recent reviews have included secondary analyses on whether the relationship between acute or long-term exercise and energy intake is influenced by physical activity level (Donnelly et al., 2014; Schubert et al., 2013). From their meta-analysis, Schubert et al. (2013) found that absolute energy intake after acute exercise was greater in active individuals compared to those less active, whereas Donnelly et al. (2014) concluded from their systematic review that increased physical activity or exercise, regardless of physical activity level, had no consistent effect on acute or long-term energy intake. However, these reviews only included energy and macronutrient intake as their main outcome measures. This limitation is of importance as appetite control involves the complex co-ordination of a range of homeostatic and non-homeostatic signals in the overall expression of food intake (Schwartz et al., 2000). Therefore, in addition to energy intake it is important to consider other components such as appetite-related peptides, subjective appetite sensations, food choice, and hedonic reward.

It has been proposed that the regulation of the appetite control system and energy intake is improved with increasing levels of physical activity (Blundell, 2011). This issue has yet to be systematically reviewed, and the potential mechanisms behind any improvement in appetite control are unclear. The aim of this systematic review was to examine whether physically active individuals have more sensitive control over appetite than their inactive counterparts and if this confers them the ability to better match energy intake to energy expenditure, and identify behavioural or physiological mechanisms underlying any observed differences.

2.2 Methods

This systematic review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and is registered in the PROSPERO database (registration number CRD42015019696).

2.2.1 Search strategy

A search was conducted in the databases Ovid Medline, Ovid Embase and SPORTDiscus (EBSCOHost), which included articles published between 1st January 1996 and 15th April 2015 using the strategy (physical activity AND (appetite AND (food intake OR appetite-related peptides))). Previous systematic reviews were screened to identify relevant subject headings and key words to include within each subject category. The specific key words used for the search are listed in Table 2-1 and the full search strategy for one of the databases consulted can be found in Appendix A.1. Limits were set to include articles published in English and studies conducted in human adults aged 18-64 years. Reference lists from the resulting articles were also screened to identify any additional articles. Articles published after 15th April 2015 that met the inclusion criteria can be found in Appendix A.3.

Table 2-1 Keywords included in database search strategy

Physical activity	**Appetite**	**Food intake**	**Appetite-related peptides**
Motor activity	Appetite	Energy intake	Gut hormone
Exercise	Feeding behavior	Diet	Gut peptide
Oxygen consumption	Food preferences	Dietary proteins	Peptide YY
Physical fitness	Hunger	Dietary fats	PYY
Exercise tolerance	Satiety	Dietary carbohydrates	Ghrelin
Exercise test	Satiation	Calorie intake	Glucagon-like peptide-1
Physical endurance	Fullness	Food intake	GLP-1
Physical activity	Motivation to eat	Meal size	Pancreatic polypeptide
Physical performance	Food choice	Energy compensation	PP
Aerobic	Food selection	Energy density	Leptin
Aerobic capacity	Desire to eat	Macronutrient	Insulin
Training	Palatability		Cholecystokinin
Maximal VO_2	Food reward		CCK
Physical capacity	Hedonic		
	Liking		
	Wanting		

2.2.2 Study selection, inclusion, and exclusion

Articles were included if they involved healthy adults participating in cross-sectional studies and examined appetite control in physically active and inactive individuals. Longitudinal studies assessing appetite control before and after an exercise-training intervention in previously inactive individuals were also included if the intervention was greater than four weeks (to allow sufficient time for adaptations from regular physical activity to emerge; e.g. (Cornelissen & Smart, 2013)) and did not include any concurrent dietary intervention (e.g. energy restriction, supplementation). Articles were excluded if they involved animals, children, adolescents, athletes or older adults (>65 years old) and participants who smoked. Abstracts and full-texts were assessed for eligibility independently by KB and a second reviewer with uncertainty regarding eligibility discussed with a third reviewer.

2.2.3 Data extraction and synthesis

The following study information was extracted into a spreadsheet: authors, date of publication, sample size, participant characteristics (age, sex, body mass index (BMI), % body fat, maximal aerobic capacity (VO_{2max}), physical activity details), criteria used to assess physical activity status (cross-sectional studies) or training intervention (longitudinal studies), setting, outcome measures (energy intake, appetite ratings and appetite-related peptides), and results. To determine any statistical relationship between habitual physical activity level and energy intake, where data were available energy intake values were standardised (*z*-scores) and from the definitions provided in the studies, physical activity levels were graded into low (<150 min/wk, <1000 kcal/wk or physical activity level (PAL): 1.4-1.69), medium (150-419 min/wk, 1000-2499 kcal/wk or PAL: 1.7-1.99), high (420-839 min/wk or 2500-3499 kcal/wk), or very high (>840 min/wk or >3500 kcal/wk). One-way ANOVA was then used to test for a main effect of graded physical activity level on energy intake score, followed by trend analyses for linear and non-linear functions. Other outcome measures are presented as a qualitative synthesis.

2.2.4 Risk of bias

Risk of bias was assessed using the Cochrane Collaboration's tool for assessing risk of bias for sequence generation, allocation concealment, blinding of participants, personnel and outcome assessors, incomplete outcome data, selective outcome reporting, and other sources of bias (Appendix A.2; Higgins & Green, 2008). Study inclusion was not influenced by the results of the risk of bias assessment.

2.3 Results

Figure 2-1 illustrates the systematic review flow diagram. The database search yielded 2,078 articles, 1,640 of which were eliminated based on titles and abstracts alone. The full text was retrieved from 77 articles and 28 satisfied the inclusion criteria. A further 13 studies were included in this thesis in Appendix A.3.

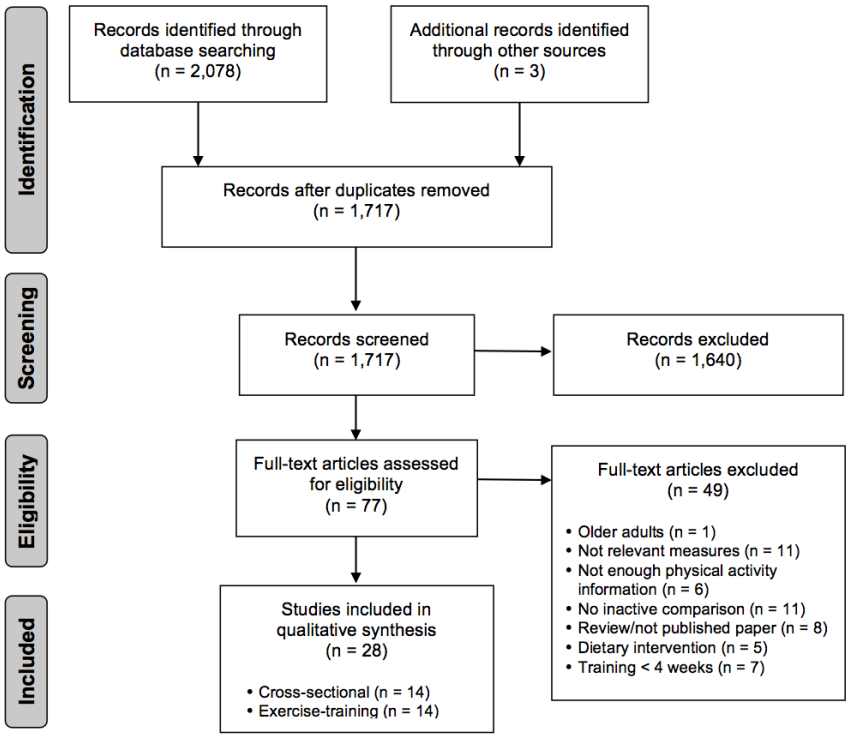

Figure 2-1 Systematic review flow diagram

2.3.1 Cross-sectional studies

The results from the cross-sectional studies (*n*=14) are presented in Table 2-2.

Table 2-2 Cross-sectional studies assessing appetite control in physically active and inactive individuals

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Apolzan et al. (2009) Young groups	Men and women Active: n = 11 (63.6 % men); age = 25±3 years; BMI = 23.5±2.0 kg/m^2; body fat =15.7±6.3 %; VO_{2max} = 47.5±6.3 mL/kg/min; PA =2.6±0.7 h/d Inactive: n = 13 (61.5% men); age = 25±4 years; BMI = 26.6±3.6 kg/m^2; body fat = 23.1±5.0 %; VO_{2max} = 33.7±5.8 mL/kg/min; PA = 0.0±0.0 h/d	Paffenbarger physical activity questionnaire and VO_{2max} Active: MVPA ≥4d/wk, VO_{2max} above average for age, >2500 kcal/wk Inactive: <20min/d ≤2 d/wk, VO_{2max} below average for age, <1000 kcal/wk	Free-living	Hunger, fullness, desire to eat (vertical dashes) Food intake (24-h food record)	No effect of activity status on appetite, energy intake or macronutrient intake.

PA, physical activity; *MVPA*, moderate-to-vigorous physical activity

Table 2-2 continued

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Catenacci et al. (2014)	Men and women enrolled in the National Weight Control Registry divided into levels of PA Low: n = 910 (21.6 % men); age = 49±13 years; BMI = 25.8±4.5 kg/m^2; body fat = NR; VO_{2max} = Not reported (NR); PA = 416±313 kcal/wk Medium: n = 934 (21.5 % men); age = 48±13 years; BMI = 25.2±4.6 kg/m^2; body fat = NR; VO_{2max} = NR; PA = 1615±355 kcal/wk High: n = 779 (26.1 % men); age = 46±12 years; BMI = 24.7±4.7 kg/m^2; body fat = NR; VO_{2max} = NR; PA = 2256±554 kcal/wk Very high: n = 968 (27.6 % men); age = 44±11 years; BMI = 24.5±4.7 kg/m^2; body fat = NR; VO_{2max} = NR; PA = 5477±2179 kcal/wk	Paffenbarger physical activity questionnaire Low: <1000 kcal/wk Medium: 1000 to <2500 kcal/wk High: 2500 to <3500 kcal/wk Very high: >3500 kcal/wk	Free-living	Food intake (Block FFQ) Restraint, disinhibition and susceptibility to hunger (TFEQ)	No significant differences in energy intake between groups but higher energy intake in those reporting the lowest and highest levels of activity (U-shaped relationship with age and sex as covariates) Higher levels of activity had lower % energy from fat and higher % energy from carbohydrates. Cognitive restraint increased with activity level (linear relationship). No differences in disinhibition and susceptibility to hunger between groups.

NR, not reported; *FFQ,* food frequency questionnaire; *TFEQ,* Three-Factor Eating Questionnaire.

Table 2-2 continued

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Charlot & Chapelot (2013)	Men High-fit: n = 9; age = 21±2 years; BMI = 23.5±0.7 kg/m^2; body fat =12.0±2.8 %; VO_{2max} = 51.6±6.1 mL/kg/min; PA = 8.8±4.5 h/wk Low-fit: n = 9; age = 22±2 years; BMI = 26.5±1.3 kg/m^2; body fat =21.2±2.6 %; VO_{2max} = 37.0±5.9 mL/kg/min; PA = 2.0±1.8 h/wk	VO_{2max} High fit: VO_{2max} > 45 and >5h/wk of MVPA. Low fit: VO_{2max} < 45 and < 3h/wk of MVPA.	Laboratory and free-living: Test meal 60-min after 60-min cycling at 70% VO_{2max}.	Hunger, desire to eat and fullness (VAS) Food intake (1 test meal and food record until breakfast the next day)	No differences in appetite ratings, energy intake at test meal, macronutrient intake, and energy compensation. Energy intake from lunch to breakfast and over 24h significantly greater after exercise compared to resting in both groups.
Deshmukh-Taskar et al. (2007)	Men and women n = 1191 (39.4 % men); age = 30±5 years; BMI = 27.3±6.7 kg/m^2; body fat = NR; VO_{2max} = NR; PA (5-point Likert scale) = 3.2±1.1	Answer to "Compared to other people your age and sex, how would you rate your physical activity outside of work during the past year?" from five-item Likert scale where 1=physically inactive/sedentary, 3=moderately active and 5=very active Active: ≥4 (n=392) Inactive: ≤3 (n=799)	Free-living	Food choices (Youth/ Adolescent FFQ)	Active reported a greater intake of fruits and 100% fruit juices and lower intake of burgers and sandwiches than inactive.

VAS, visual analogue scale.

Table 2-2 continued

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Georgiou et al. (1996)	Men Exercisers: n = 89; age = 22±2 years; BMI = 24.8±4.1 kg/m^2; body fat = NR; VO_{2max} = NR; PA = NR Nonexercisers: n = 51; age = 22±2 years; BMI = 25.7±5.2 kg/m^2; body fat = NR; VO_{2max} = NR; PA = NR Women Exercisers: n = 106; age = 21±2 years; BMI = 22.3±3.6 kg/m^2; body fat = NR; VO_{2max} = NR; PA = NR Nonexercisers: n = 73; age = 22±2 years; BMI = 22.8±4.1 kg/m^2; body fat = NR; VO_{2max} = NR; PA = NR	Yes or no response to "Do you engage in regular, planned exercise activities in which you work up a sweat, increase your heart rate or breathe faster?"	Free-living	Food choices (National Cancer Institute Health Habits and History Questionnaire FFQ) Health-related influences on food choice questionnaire Perceived change of fat intake	Female and male exercisers considered it more important to eat the most nutritious foods than nonexercisers. Female and male exercisers ate more nutrient-dense, low-fat foods than nonexercisers. Female exercisers were more likely to rate 2% milk, macaroni and cheese, hamburger, and peanut butter as fattening compared to nonexercisers. Female exercisers reported decreasing intake of high-fat foods (e.g. French fries, cheese and salad dressing) over the prior years.
Gregersen et al. (2011)	Men n = 80; age = 39±12 years; BMI = 25.2±2.7 kg/m^2; body fat = NR; VO_{2max} = NR; PA = NR Women n = 98; age = 41±11 years; BMI = 24.4±3.0 kg/m^2; body fat = NR; VO_{2max} = NR; PA = NR	Self-reported physical activity level (Subgroup analysis) High/moderate exercise (n =46): training hard ≥4 hr/wk Light/no exercise (n =129): light exercise <4 hr/wk	Laboratory: Standardized evening meal to 35% of individual daily energy requirement.	Hunger, fullness, satiety, PFC (VAS) pre and over 3h post-meal. Palatability	Hard/moderate exercisers had lower mean ratings of post-prandial satiety and higher mean ratings of post-meal hunger and PFC than light/non-exercisers. (Differences became non-significant when age and sex added as covariates.) No differences in palatability between groups.

PFC, prospective food consumption.

Table 2-2 continued

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Harrington et al. (2013)	Non-obese men n = 40; age = 27±4 years; BMI = 23.5±2.5 kg/m^2; body fat = NR; VO_{2max} = NR; PA = NR Non-obese women n = 42; age = 27±5 years; BMI = 22.4±2.0 kg/m^2; body fat = NR; VO_{2max} = NR; PA = NR	Activity-related energy expenditure derived from the residual value of the regression between TDEE from doubly-labelled water and 24-h resting energy expenditure. Activity-related energy expenditure divided into low, middle and high tertiles.	Laboratory	Food intake (test meal) Hunger, fullness, desire to eat and PFC (VAS) pre and post-test meal. SQ	Males in low tertile significantly higher fasting desire to eat, PFC and lower fullness than high tertile. No differences in fasting appetite between groups in women. No differences in appetite ratings after the test meal between groups in both men and women. Males in middle tertile had a significantly lower energy intake than high tertile and tended to have lower energy intake than low tertile. Males in high tertile had a significantly lower SQ for each appetite rating compared to middle tertile.

SQ, satiety quotient.

Table 2-2 continued

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Jago et al. (2005)	Men and women n = 1191 (39.3 % men); age = 30±5 years; BMI = 27.3±6.7 kg/m^2; body fat = NR; VO_{2max} = NR; PA (5-point Likert scale) = 3.2±1.1 Group 1: n=74; Group 2: n=181; Group 3: n=544; Group 4: n=180, Group 5: n=212	Answer to "Compared to other people your age and sex, how would you rate your physical activity outside of work during the past year?" from five-item Likert scale where 1=physically inactive/sedentary, 3=moderately active and 5=very active	Free-living	Food intake (Youth/ Adolescent FFQ)	Groups 3, 4, and 5 reported greater intake of dairy products than group 1. Groups 3, 4 and 5 consumed fewer servings of fried foods than group 2. Group 5 had a greater energy intake than group 3 but no differences were seen with the other groups. Group 2 consumed greater % energy from fat than group 4.
Jokisch et al. (2012)	Men Active: n = 10; age = 21±2 years; BMI = 23.9±1.5 kg/m^2; body fat = 12.6±2.8 %; VO_{2max} = NR; PA = 438±152 min/wk Inactive: n = 10; age = 21±2 years; BMI = 23.0±1.9 kg/m^2; body fat = 15.0±2.3 %; VO_{2max} = NR; PA = 32±43 min/wk	Seven-day physical activity recall x 2 Active: ≥ 150min/wk MVPA Inactive: ≤ 60min/wk MVPA	Laboratory: Test meal 60-min after 45-min cycling at 65-75% HR_{max} or rest.	Hunger and liking (VAS) Food intake (1 test meal and food record for remainder of the day)	Inactive had greater energy intake at test meal after rest than exercise. Both groups had greater energy intake after exercise compared to rest. Tendency for inactive to have greater energy intake than active. No differences in macronutrient intake at test meal but active consumed greater % energy from protein vs. inactive during remainder of day. Difference in energy compensation between groups (positive in active and negative in inactive) at test meal, but no differences in energy compensation for remainder of the day.

HR_{max}, maximal heart rate.

Table 2-2 continued

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Long et al. (2002)	Men High exercisers: n = 7; age = 22±3 years; BMI = 22.5±1.5 kg/m^2; body fat = NR; VO_{2max} = NR; PA = NR Moderate exercisers: n = 7; age = 27±7 years; BMI = 24.1±3.6 kg/m^2; body fat = NR; VO_{2max} = NR; PA = NR Nonexercisers: n = 9; age = 22±2 years; BMI = 24.1±3.6 kg/m^2; body fat = NR; VO_{2max} = NR; PA = NR	Seven-day physical activity recall x 2 High exercisers: ≥4 exercise sessions/wk Moderate exercisers: 2-3 exercise sessions/wk Nonexercisers: ≤1 exercise session/wk Exercise session: ≥40 min MVPA	Laboratory: LE preload and HE preload followed by test meal.	Hunger and satiety (VAS) Food intake (1 test meal)	Energy intake in exercisers (groups combined) significantly less after HE vs. LE preload. Energy intake after HE preload significantly lower in exercisers vs. nonexercisers. Energy compensation more accurate in active vs. inactive. Hunger before preload significantly higher in nonexercisers under both HE and LE preloads but no other differences in appetite ratings.
Lund et al. (2013)	Men Trained: n = 10; age = 26±3 years; BMI = 22±3 kg/m^2; body fat = 12±3 %; VO_{2max} = 67±6 mL/kg/min; PA = NR Untrained: n = 10; age = 25±3 years; BMI = 22±3 kg/m^2; body fat = 21±3 %; VO_{2max} = 42±6 mL/kg/min; PA = NR	VO_{2max} Trained: Aerobic endurance exercise >3d/wk over several years and VO_{2max} > 60 mL/kg/min (runners, cyclists or triathletes) Untrained: No exercise during last 6 months and VO_{2max} < 50 mL/kg/min	Laboratory: Liquid meal followed by test meal 3 h later	Hunger, satiety, fullness and PFC (VAS) Meal size (test meal) GLP-1, insulin, AG, PYY, PP	GLP-1 and AG higher at baseline in trained. GLP-1 higher and insulin lower following liquid meal in trained. No group differences in PYY and PP at baseline and in response to liquid meal. No group differences in appetite ratings. Tendency for greater meal size (grams) in trained vs. untrained, significant after removal of outlier in untrained group.

LE, low-energy; *HE*, high-energy; *AG*, acylated ghrelin; *PP*, pancreatic polypeptide.

Table 2-2 continued

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Rocha et al. (2013)	Men Active: n = 15; age = 23±4 years; BMI = 22.6±2.0 kg/m^2; body fat = 14.3±3.4 %; VO_{2max} = 44.6±5.0 mL/kg/min; PAL (TDEE/BMR) = 1.80±0.19 Inactive: n = 15; age = 24±3 years; BMI = 25.1±2.4 kg/m^2; body fat = 22.2±3.8 %; VO_{2max} = 35.5±5.2 mL/kg/min; PAL = 1.54±0.19	Modified Godin leisure-time exercise questionnaire PA monitor (Actiheart) Active: Regular exercisers and >150 min/wk of MVPA and PAL 1.70-1.99 Inactive: Did not engage in regular exercise and <150 min/wk of MVPA and PAL 1.4-1.69	Laboratory and free-living: Test meal following 60-min cycling at 50% VO_{2max} or rest.	Hunger (VAS) Food intake (1 test meal and food record for remainder of the day and subsequent 3 days)	No effects on hunger and energy intake at test meal. Active had greater energy intake during exercise day than rest day. Inactive increased energy intake on 3rd day after exercise compared to rest. Energy compensation observed in active but not inactive during experimental day.
Rocha et al. (2015)	Women taking oral contraceptives Active: n = 10; age = 23±4 years; BMI = 21.9±1.3 kg/m^2; body fat = 22.5±3.7 %; VO_{2max} = 36.8±3.1 mL/kg/min; PA level (TDEE/BMR) = 1.79±0.13 Inactive: n = 10; age = 22±3 years; BMI = 21.6±2.0 kg/m^2; body fat = 26.7±3.6 %; VO_{2max} = 29.9±4.1 mL/kg/min; PAL = 1.56±0.15	Modified Godin leisure-time exercise questionnaire Physical activity monitor (Actiheart) Active: Regular exercisers and >150 min/wk of MVPA and PAL 1.70-1.99 Inactive: Not regular exercisers and <150 min/wk of MVPA and PAL 1.4-1.69	Laboratory and free-living: Test meal following 60-min cycling at 50% VO_{2max} or rest.	Hunger (VAS) Food intake (1 test meal and food record for remainder of the day and subsequent 3 days)	No group differences in hunger, energy intake at test meal or macronutrient intake. Inactive had greater energy intake over the four days than active. Inactive had lower daily energy intake the day following exercise compared to rest. No energy compensation observed.

Table 2-2 continued

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Van Walleghen et al. (2007) Young groups	Men and women Active: n = 15 (45.4 % men); age = 23±4 years; BMI = 23.1±2.7 kg/m^2; body fat = 18.2±8.5 %; VO_{2max} = 55.6±10.5 mL/kg/min; PA = 575±406 min/wk Inactive: n = 14 (50 % men); age = 26±4 years; BMI = 23.5±3.0 kg/m^2; body fat = 27.2±5.6 %; VO_{2max} = 37.9±7.1 mL/kg/min; PA = 16±37 min/wk	Self-reported time spent doing MVPA Active: ≥150min/wk MVPA for ≥ 2 yr Inactive: NR	Laboratory and free-living: Preload or no preload followed by test meal.	Hunger and fullness (VAS) Food intake (1 test meal and food record for remainder of the day) Fasting insulin and insulin sensitivity	Active had greater habitual energy intake, lower % energy from fat and greater % energy from carbohydrate than inactive. No group differences in appetite or energy intake at test meal. Active had greater energy intake than inactive during the remainder of the day in no preload condition. No group differences for energy compensation at test meal, but compensation over the entire day was significantly more accurate in active vs. inactive subjects.

2.3.1.1 Study characteristics: Physical activity definitions

The median (range) sample size of the included studies was 15 (7-968) for the active group and 14 (9-910) for the inactive group. Men and women were included in eight studies, of which the median percentage of men was 42.2 (21.5-63.6) % in the active group and 50 (21.6-61.6) % in the inactive group (Apolzan et al., 2009; Catenacci et al., 2014; Deshmukh-Taskar, Nicklas, Yang, & Berenson, 2007; Georgiou, Betts, Hoos, & Glenn, 1996; Gregersen et al., 2011; Harrington, Martin, Ravussin, & Katzmarzyk, 2013; Jago et al., 2005; Van Walleghen, Orr, Gentile, Davy, & Davy, 2007). Five studies included only men (Charlot & Chapelot, 2013; Jokisch, Coletta, & Raynor, 2012; Long et al., 2002; Lund et al., 2013; Rocha, Paxman, Dalton, Winter, & Broom, 2013) and one study included only women (Rocha, Paxman, Dalton, Winter, & Broom, 2015).

Physical activity status was determined by self-report (physical activity questionnaire, physical activity level question or physical activity recall) in 11 studies (Catenacci et al., 2014; Deshmukh-Taskar et al., 2007; Georgiou et al., 1996; Gregersen et al., 2011; Jago et al., 2005; Jokisch et al., 2012; Long et al., 2002; Van Walleghen et al., 2007), a VO_{2max} test in three studies (Apolzan et al., 2009; Charlot & Chapelot, 2013; Lund et al., 2013), or from TDEE and resting energy expenditure or basal metabolic rate (BMR) in three studies (Harrington et al., 2013; Rocha et al., 2013, 2015). Only three studies used a combination of self-reported and objectively-measured physical activity status (Apolzan et al., 2009; Rocha et al., 2013, 2015).

The active groups were defined as participating in moderate-to-vigorous physical activity (MVPA) for at least: 150 min/wk (Jokisch et al., 2012; Rocha et al., 2013, 2015; Van Walleghen et al., 2007), 4 h/wk (Gregersen et al., 2011), 5 h/wk with a VO_{2max} greater than 45mL/kg/min (Charlot & Chapelot, 2013), 3 d/wk with a VO_{2max} greater than 60mL/kg/min (Lund et al., 2013), 4 d/wk and >2500kcal/wk with a VO_{2max} above average for age (Apolzan et al., 2009), or 1000kcal/wk (Catenacci et al., 2014). A PAL (TDEE/BMR) value between 1.70-1.99 was utilised in two studies (Rocha et al., 2013, 2015). Moderate exercisers participated in 2 to 3 sessions/wk of at least 40 min of MVPA (Long et al., 2002) or expended between 1000-2499 kcal/wk (Catenacci et al., 2014). High exercisers participated in 4 or more structured exercise sessions/wk of at least 40 minutes of MVPA (Long et al., 2002) or expended 2500-3499 kcal/wk (Catenacci et al., 2014), whereas very high exercisers expended greater than 3500 kcal/wk (Catenacci et al., 2014).

The inactive groups were defined as no exercise over the previous 6 months and VO_{2max} less than 50 mL/kg/min (Lund et al., 2013) or less than: 1 session/wk of MVPA (Long et al., 2002), 20 min/d and 2 d/wk (Apolzan et al., 2009), 60 min/wk (Jokisch et al., 2012), 1000 kcal/wk (Catenacci et al., 2014), 150 min/wk of MVPA

(Rocha et al., 2013, 2015), 3 h/wk of MVPA with a VO_{2max} less than 45 mL/kg/min (Charlot & Chapelot, 2013), or 4 h/wk (Gregersen et al., 2011). Two studies used a PAL value between 1.4-1.69 (Rocha et al., 2013, 2015).

Based on the physical activity definitions above, for the purposes of statistical treatment, four physical activity levels were distinguished as low (<150 min/wk, <1000 kcal/wk or PAL: 1.4-1.69), medium (150-419 min/wk, 1000-2499 kcal/wk or PAL: 1.7-1.99), high (420-839 min/wk or 2500-3499 kcal/wk) and very high (>840 min/wk or >3500 kcal/wk) for analysis of standardised energy intake.

2.3.1.2 Study characteristics: Appetite-related measures

Five studies evaluated appetite measures in a laboratory (Gregersen et al., 2011; Harrington et al., 2013; Jokisch et al., 2012; Long et al., 2002; Lund et al., 2013), five studies in free-living conditions (Apolzan et al., 2009; Catenacci et al., 2014; Deshmukh-Taskar et al., 2007; Georgiou et al., 1996; Jago et al., 2005), and four studies combined laboratory and free-living measures (Charlot & Chapelot, 2013; Rocha et al., 2013, 2015; Van Walleghen et al., 2007). Four studies included exercise (45-60 min cycling at 50-75 % VO_{2max} or HR_{max}) during the laboratory session (Charlot & Chapelot, 2013; Jokisch et al., 2012; Rocha et al., 2013, 2015). Ten studies included fasting and/or daily (area under the curve; AUC) subjective appetite ratings, all of which included hunger (Apolzan et al., 2009; Charlot & Chapelot, 2013; Gregersen et al., 2011; Harrington et al., 2013; Jokisch et al., 2012; Long et al., 2002; Lund et al., 2013; Rocha et al., 2013, 2015; Van Walleghen et al., 2007). Other appetite ratings assessed were fullness (Apolzan et al., 2009; Charlot & Chapelot, 2013; Gregersen et al., 2011; Harrington et al., 2013; Jokisch et al., 2012; Lund et al., 2013; Van Walleghen et al., 2007), prospective food consumption (PFC) (Gregersen et al., 2011; Harrington et al., 2013; Lund et al., 2013), desire to eat (Apolzan et al., 2009; Charlot & Chapelot, 2013; Harrington et al., 2013), satiety (Gregersen et al., 2011; Long et al., 2002; Lund et al., 2013), liking (Jokisch et al., 2012) and palatability (Gregersen et al., 2011). One study reported restraint, disinhibition and susceptibility to hunger (Catenacci et al., 2014). Eleven studies assessed energy intake, either via a food frequency questionnaire (FFQ) (Catenacci et al., 2014; Jago et al., 2005), food record (Apolzan et al., 2009), laboratory-based test meals (Harrington et al., 2013; Long et al., 2002; Lund et al., 2013), or a combination of laboratory-based test meals and food records (Charlot & Chapelot, 2013; Jokisch et al., 2012; Rocha et al., 2013, 2015; Van Walleghen et al., 2007). Six studies reported energy compensation following either a preload (Long et al., 2002; Van Walleghen et al., 2007) or a single bout of exercise (Charlot & Chapelot, 2013; Jokisch et al., 2012; Rocha et al., 2013, 2015). Eight studies reported macronutrient intake (Apolzan et al., 2009; Catenacci et al., 2014;

Charlot & Chapelot, 2013; Jago et al., 2005; Jokisch et al., 2012; Rocha et al., 2013, 2015; Van Walleghen et al., 2007). Three studies assessed food choices via FFQ (Deshmukh-Taskar et al., 2007; Georgiou et al., 1996; Jago et al., 2005). Two studies included the assessment of appetite-related peptides (Lund et al., 2013; Van Walleghen et al., 2007).

2.3.1.3 Participant characteristics

The median (range) age was 23 (21-48) years for the active groups and 22 (21-49) years for the inactive groups.

In the 10 studies that reported BMI of the active and inactive groups separately, the median (range) was 23.5 (21.9-25.2) kg/m^2 for the active group and 24.1 (21.6-26.6) kg/m^2 for the inactive group (Apolzan et al., 2009; Catenacci et al., 2014; Charlot & Chapelot, 2013; Georgiou et al., 1996; Jokisch et al., 2012; Long et al., 2002; Lund et al., 2013; Rocha et al., 2013, 2015; Van Walleghen et al., 2007). In three studies, the inactive group had a significantly greater BMI than the active group (Apolzan et al., 2009; Charlot & Chapelot, 2013; Rocha et al., 2013). In those that reported BMI of the groups combined, the median (range) was 24.8 (22.4-27.3) kg/m^2 (Deshmukh-Taskar et al., 2007; Gregersen et al., 2011; Harrington et al., 2013; Jago et al., 2005).

In the seven studies that reported percent body fat, the median (range) was 14.3 (12.0-22.5) % for the active group and 22.2 (15.0-27.2) % for the inactive group (Apolzan et al., 2009; Charlot & Chapelot, 2013; Jokisch et al., 2012; Lund et al., 2013; Rocha et al., 2013, 2015; Van Walleghen et al., 2007). In all studies, the inactive group had a significantly greater percent body fat than the active group.

In the six studies that reported VO_{2max}, the median (range) was 49.6 (36.8-67.0) mL/kg/min for the active group and 36.3 (29.9-42.0) mL/kg/min for the inactive group (Apolzan et al., 2009; Charlot & Chapelot, 2013; Lund et al., 2013; Rocha et al., 2013, 2015; Van Walleghen et al., 2007). In all studies, the active group had a significantly greater VO_{2max} than the inactive group.

2.3.1.4 Study results: Appetite ratings

Of the 10 studies that measured appetite ratings, three found differences between the physically active and inactive groups. Harrington et al. (2013) reported greater fasting appetite and lower satiety quotient (SQ; (pre-meal appetite rating-post meal appetite rating)/energy intake) for hunger, fullness, desire to eat and PFC in men in the high activity tertile compared to the moderate activity tertile, whereas Long et al. (2002)

reported greater fasting appetite in the inactive group. Gregersen et al. (2011) found greater post-prandial appetite in the active group, however differences became non-significant when age and sex were added as covariates.

2.3.1.5 Study results: Energy and macronutrient intake

Ten of eleven studies found differences in energy intake between active and inactive individuals. Two studies found greater energy intake (habitual energy intake (Van Walleghen et al., 2007) or at a test meal (Lund et al., 2013)) in the active compared to the inactive group, whereas one study observed greater energy intake in inactive women over four days than active women (Rocha et al., 2015). Furthermore, two studies observed a non-linear relationship in energy intake, whereby energy intake was highest in the groups with the lowest and highest levels of physical activity (Catenacci et al., 2014; Harrington et al., 2013), while Jago et al. (2005) only observed a greater energy intake in the very active group compared to the moderately active group. In studies assessing energy intake following a preload, Long et al. (2002) found that energy intake at an ad libitum test meal following a high-energy preload was significantly lower than following the low-energy preload in regular exercisers. The same study showed that compared to nonexercisers, energy intake following the high-energy preload was significantly lower in exercisers. Moreover, Van Walleghen et al. (2007) found that the active group consumed more throughout the day following the no preload condition than the inactive group, leading to significantly more accurate short-term energy compensation. Of note, however, there were no differences in energy compensation between groups at the test meal after the preload (Van Walleghen et al., 2007). In studies measuring energy intake after exercise, two of three studies in men observed energy compensation in the active group, where energy intake following an exercise session was greater compared to rest at test meal (Jokisch et al., 2012) or throughout the day (but not at the test meal in this study) (Rocha et al., 2013). One of these studies observed negative energy compensation in the inactive group, where energy intake was lower following the exercise session compared to rest, suggesting an effect of exercise-induced anorexia (Jokisch et al., 2012). Of the above studies that observed differences between groups, only four were based on objectively-measured (test meal) energy intake (Harrington et al., 2013; Jokisch et al., 2012; Long et al., 2002; Lund et al., 2013).

As for macronutrient intake, compared to the inactive group, two studies found that the active group consumed a greater percent energy from carbohydrates (Catenacci et al., 2014; Van Walleghen et al., 2007), three found lower percent energy from fat (Catenacci et al., 2014; Jago et al., 2005; Van Walleghen et al., 2007), while

one study found a greater percent energy from protein (Jokisch et al., 2012). In terms of food choices, active individuals reported a greater intake of nutrient-dense, low-fat foods (Georgiou et al., 1996), fruits and 100% fruit juices (Deshmukh-Taskar et al., 2007), and dairy products (Jago et al., 2005), and a lower intake of burgers and sandwiches (Deshmukh-Taskar et al., 2007) and fried foods (Jago et al., 2005) than inactive.

2.3.1.6 Study results: Standardized energy intake

To further examine the relationship between energy intake and physical activity level, the available energy intake data from the cross-sectional studies (Apolzan et al., 2009; Catenacci et al., 2014; Charlot & Chapelot, 2013; Harrington et al., 2013; Jago et al., 2005; Jokisch et al., 2012; Lund et al., 2013; Rocha et al., 2013, 2015; Van Walleghen et al., 2007) were extracted and transformed into standardized scores then plotted according to their reassigned physical activity levels (low, medium, high, very high) as described in Section 2.3.1.1. In the studies that included a preload or an exercise bout (Charlot & Chapelot, 2013; Jokisch et al., 2012; Rocha et al., 2013, 2015), energy intake was taken from the control condition. Of these 10 studies, eight were based on self-reported daily energy intake (Apolzan et al., 2009; Catenacci et al., 2014; Charlot & Chapelot, 2013; Jago et al., 2005; Jokisch et al., 2012; Rocha et al., 2013, 2015; Van Walleghen et al., 2007) while two were based on energy intake at a test meal (Harrington et al., 2013; Lund et al., 2013). The pattern of means revealed a J-shaped curve for energy intake as habitual physical activity level increased (Figure 2-2). One-way ANOVA confirmed a main effect of graded physical activity level on energy intake score ($F(3,21)=3.57$, $p=.03$). Post hoc trend analyses revealed significant effects for linear ($F=5.79$, $p=.03$) and curvilinear (quadratic) ($F=8.10$, $p=.01$) functions.

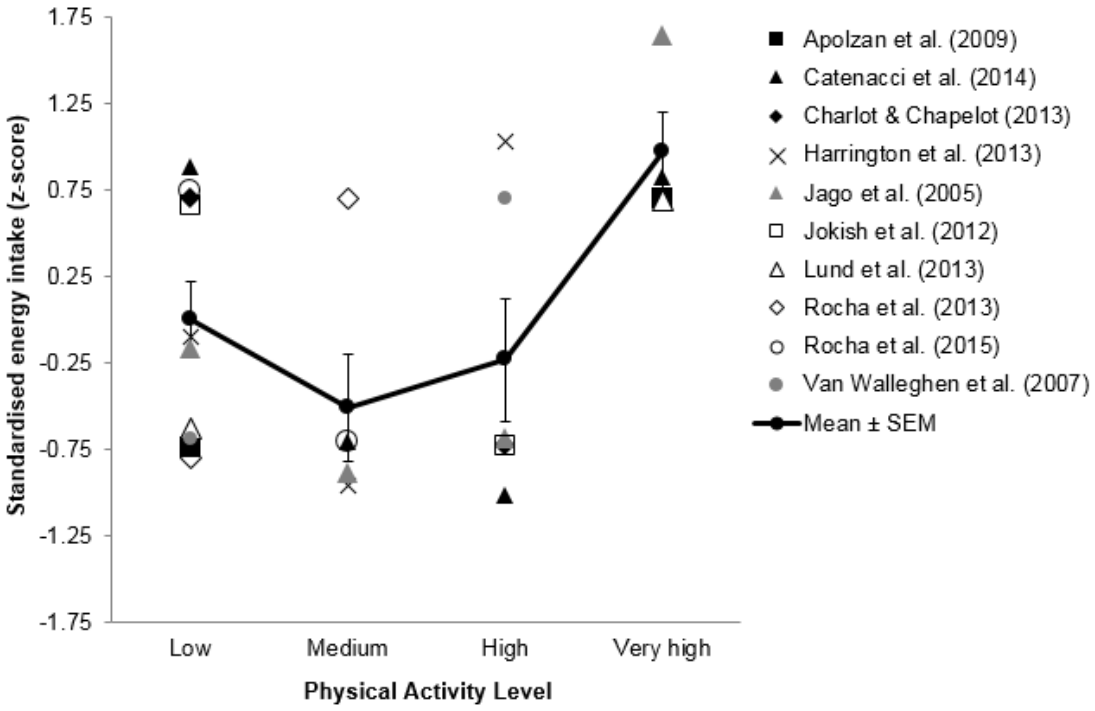

Figure 2-2 Standardised energy intake by physical activity level from the 10 cross-sectional studies reporting energy intake (*n*=25 data points). Trend analysis confirmed significant linear ($p<0.05$) and quadratic ($p<0.01$) relationship between graded physical activity level and energy intake scores. Black line indicates mean of the z-scores; *SEM,* standard error of the mean.

2.3.1.7 Study results: Appetite-related peptides

Van Walleghen et al. (2007) found greater insulin sensitivity in the active group. Lund et al. (2013) found that in active individuals, GLP-1 and acylated ghrelin were higher at baseline (insulin tended to be lower), and following a liquid meal, GLP-1 was higher and insulin was lower in active. No group differences were found for PYY and pancreatic polypeptide.

2.3.2 Exercise-training interventions

The results from the exercise-training interventions (*n*=14) are presented in Table 2-3.

Table 2-3 Studies investigating the effect of exercise training on appetite control in previously inactive individuals

Study	Participants	Training intervention	Setting	Outcome measures	Results
Alkahtani et al. (2014)	Overweight and obese men n = 10; age = 29±4 years; BMI baseline = 30.7±3.4 kg/m^2; BMI post = NR; body fat baseline = 31.2±4.7 %; body fat post = NR; VO_{2max} baseline = 28.7±3.4 mL/kg/min; VO_{2max} post = NR	4 wk supervised MIIT 3d/wk (30-45 min of 5-min stages at ±20% workload at 45%VO_{2peak}) 4 wk supervised HIIT 3d/wk (30-45 min of 30-s 90%VO_{2peak} and 30-s rest) Each training block was counterbalanced and separated by a 6-week detraining washout	Laboratory: Test meal following 45-min cycling at 45% VO_{2max} at pre and post both training blocks.	Hunger, desire to eat and fullness (VAS) Liking and wanting (computer-based paradigm) Food intake (test meal)	Tendency for suppression of desire to eat after acute exercise post-training with HIIT compared to MIIT. Tendency for increase with MIIT and decrease with HIIT in explicit liking for high-fat non-sweet foods after acute exercise post-training. No effects of training on food intake or energy intake. Tendency for fat intake and % energy from fat to increase after MIIT.
Bryant et al. (2012)	Overweight and obese men and women n = 58 (32.7 % men); age = 36±10 years; BMI baseline = 31.8±4.5 kg/m^2; BMI post = 30.7±4.4 kg/m^2; body fat baseline = 34.8±7.8 %; body fat post = 31.9±9.0 %; VO_{2max} baseline = 29.1±5.7 mL/kg/min; VO_{2max} post = NR	12 wk supervised aerobic exercise 5d/wk (500kcal at 70% HR_{max})	Laboratory	Food intake (Self-determined fixed breakfast followed by 2 ad libitum meals and evening snack box) Restraint, disinhibition and susceptibility to hunger (TFEQ)	No change in 24-h energy intake or susceptibility to hunger. Significant reduction in disinhibition and increase in restraint after training.

MIIT, moderate-intensity interval training; *HIIT*, high-intensity interval training.

Table 2-3 continued

Study	Participants	Training intervention	Setting	Outcome measures	Results
Caudwell et al. (2013)	Overweight and obese men n = 14; age = 44±6 years; BMI baseline = 31.3±5.0 kg/m^2; BMI post = 30.5±4.9 kg/m^2; body fat baseline = 34.3±7.0 %; body fat post = 32.4±7.6 %; VO_{2max} = NR Overweight and obese premenopausal women n = 27; age = 42±8 years; BMI baseline = 30.4±3.2 kg/m^2; BMI post = 30.2±3.6 kg/m^2; body fat baseline = 44.0±5.5 %; body fat post = 42.5±5.8 %; VO_{2max} = NR	12 wk supervised aerobic exercise 5d/wk (500kcal at 70% HR_{max})	Laboratory: HE and LE density probe days.	Food intake (Self-determined fixed breakfast, fixed energy lunch and ad libitum dinner and evening snack box)	Significant main effect of training on HE density meal size (reduction) but not LE density meal size. No main effect of training on daily energy intake under each dietary condition.

Table 2-3 continued

Study	Participants	Training intervention	Setting	Outcome measures	Results
Caudwell et al. (2013)	Overweight and obese men n = 35; age = 41±9 years; BMI baseline = 30.5±8.6 kg/m^2; BMI post = 29.6±1.1 kg/m^2; body fat baseline = 33.8±6.6 %; body fat post = 31.3±3.3 %; VO_{2max} baseline = 34.9±6.9 mL/kg/min, VO_{2max} post = 43.3±6.9 mL/kg/min Overweight and obese premenopausal women n = 72; age = 41±10 years; BMI baseline = 31.8±4.3 kg/m^2; BMI post = 30.9±1.1 kg/m^2; body fat baseline = 44.1±6.0 %; body fat post = 41.6±2.2 %; VO_{2max} baseline = 29.1±6.5 mL/kg/min; VO_{2max} post = 35.1±5.5 mL/kg/min	12 wk supervised aerobic exercise 5d/wk (500kcal at 70% HR_{max})	Laboratory	Hunger, fullness and desire to eat (VAS) SQ Food intake (Self-determined fixed breakfast, fixed energy lunch and ad libitum dinner and evening snack box)	No change in 24-h energy intake with training. Significant increase in fasting hunger but no change in daily hunger AUC. SQ significantly greater post-training.

Table 2-3 continued

Study	Participants	Training intervention	Setting	Outcome measures	Results
Cornier et al. (2012)	Overweight and obese men and women n = 12 (41.6 % men); age = 38±10 years; BMI baseline = 33.3±4.3 kg/m^2; BMI post = NR; body fat baseline = 36.5±1.9 %; body fat post = 34.4±2.0 %; VO_{2max} = NR	6 months supervised treadmill walking 5d/wk (building up to 500kcal/d at 75% VO_{2max})	Laboratory and free-living: Test meal breakfast (30% estimated daily energy needs)	Leptin TFEQ, Power of Food Scale, Craving and Mood Questionnaire, Food Craving Inventory Hunger, satiety and PFC (VAS) Food intake (3-day food record)	Significant reduction in fasting leptin post-training. No change in dietary restraint or disinhibition, food cravings, Power of Food Scale, food desire and appeal, or post-prandial appetite ratings. Self-reported energy intake lower after training compared to baseline but no change in macronutrient intake.
Guelfi et al. (2013) Exercise groups	Overweight and obese men (age = 49±7 years) Aerobic training: n = 12; BMI baseline = 31.7±3.5 kg/m^2; BMI post = 31.1±3.3 kg/m^2; body fat = NR; VO_{2max} baseline = 2.25±0.51 L/min @ 80% HR_{max}; VO_{2max} post = 2.82±0.60 L/min @ 80% HR_{max} Resistance training: n = 13; BMI baseline = 30.3±3.5 kg/m^2; BMI post = 30.3±3.7 kg/m^2; body fat = NR; VO_{2max} baseline = 1.94±0.39 L/min @ 80% HR_{max}; VO_{2max} post = 2.17±0.54 L/min @ 80% HR_{max}	12 wk supervised (3d/wk) aerobic exercise (40-60 min at 70-80% HR_{max}) or resistance exercise (weight training matched for duration and intensity; 3-4 sets 8-10 repetitions of 9 exercises at 75-85% 1 repetition maximum)	Laboratory: 2-h, 75-g oral glucose tolerance test	Hunger and fullness (VAS) AG, leptin, insulin, insulin sensitivity, PP and PYY	Significant increase in fasting and postprandial fullness following aerobic training only. No change in fasting or postprandial hunger with training. Fasting and postprandial leptin were significantly lower after training. Postprandial insulin was significantly lower after aerobic training only. No change in fasting insulin, or fasting and postprandial AG, PP and PYY post-training. Improvement in insulin sensitivity in both groups post-training.

Table 2-3 continued

Study	Participants	Training intervention	Setting	Outcome measures	Results
Jakicic et al. (2011) Exercise groups	Overweight women Moderate-dose: n = 76; age = 44±8 years; BMI baseline = 27.2±1.8 kg/m^2; BMI post = 26.9±2.1 kg/m^2; body fat baseline = 33.5±4.1 %; body fat post = 33.3±4.8 %; VO_{2max} = NR High-dose: n = 88; age = 46±8 years; BMI baseline = 27.0±1.6 kg/m^2; BMI post = 26.7±2.4 kg/m^2; body fat baseline = 33.0±4.1 %; body fat post = 32.3±5.3 %; VO_{2max} = NR	18 months unsupervised moderate-dose (150min/wk), high-dose (300min/wk) ~5d/wk bouts ≥10min moderate to vigorous intensity (55-85% HR_{max})	Free-living	Food intake (FFQ) Eating Behaviour Inventory	No group by time interaction on energy intake or macronutrient intake. Eating behaviour score improved post-intervention but no differences between groups.
King et al. (2008)	Overweight and obese men and women Compensators: n = 18 (23.5 % men); age = 38±9 years; BMI baseline = 30.7±2.9 kg/m^2; BMI post = NR; body fat baseline = 32.7±8.0 %; body fat post = NR; VO_{2max} baseline = 28.8±5.7 mL/kg/min; VO_{2max} post = NR Noncompensators: n = 17 (33.3 % men); age = 40±13 years; BMI baseline = 33.1±4.7 kg/m^2; BMI post = NR; body fat baseline = 37.2±7.9 %; body fat post = NR; VO_{2max} baseline = 28.4±5.8 mL/kg/min; VO_{2max} post = NR	12 wk supervised aerobic exercise 5d/wk (500kcal at 70% HR_{max})	Laboratory	Hunger, fullness, PFC and desire to eat (VAS) Food intake (Self-determined fixed breakfast followed by 2 ad libitum meals and an evening snack box)	No significant changes in 24-h energy intake in pooled data with training, however compensators increased energy intake and % energy from fat and non-compensators decreased energy intake from baseline to post-intervention. Compensators had greater hunger profile post-training than non-compensators.

Table 2-3 continued

Study	Participants	Training intervention	Setting	Outcome measures	Results
King et al. (2009)	Overweight and obese men and women divided into responders (n=32) and non-responders (n=26) to exercise-induced weight loss n = 58 (32.7 % men); age = 40±10 years; BMI baseline = 31.8±4.5 kg/m^2; BMI post = NR; body fat = NR; VO_{2max} baseline = 29.1±5.7 mL/kg/min; VO_{2max} post = NR	12 wk supervised aerobic exercise 5d/wk (500kcal at 70% HR_{max})	Laboratory: Self-determined fixed breakfast	Hunger, fullness, PFC and desire to eat (VAS) SQ	Nonresponders and responders had significantly greater fasting hunger but also had a greater SQ post-training Only nonresponders increased daily motivation to eat (greater hunger, desire to eat and lower fullness) post-training.
Martins et al. (2007)	Men and women n = 25 (44 % men); age = 30±12 years; BMI baseline = 22.7±2.3 kg/m^2; BMI post = 22.8±2.2 kg/m^2; body fat baseline = 23.6±7.8 %; body fat post = 23.0±7.5 %; VO_{2max} baseline = 31.1±4.8 mL/kg/min; VO_{2max} post = 34.3±7.4 mL/kg/min	6 wk unsupervised aerobic exercise ≥4d/wk, 30-45min (continuously or bouts ≥10min each) at 65-75% HR_{max}	Laboratory and free-living: LE preload and HE preload	Hunger, fullness, palatability (VAS) Food intake (1 test meal and food record until breakfast next morning) Fasting insulin and insulin sensitivity	Test meal size and cumulative 24-h energy intake significantly lower following HE preload vs. LE preload post-training. No improvement in energy compensation at test meal but tendency for improved compensation over 24h. Greater % energy from protein at test meal after training. No change in fasting insulin or insulin sensitivity. No change in appetite ratings.

Table 2-3 continued

Study	Participants	Training intervention	Setting	Outcome measures	Results
Martins et al. (2010)	Overweight and obese men and women n =15 (53.3 % men); age = 37±8 years; BMI baseline = 31.3±2.3 kg/m^2; BMI post = 30.1±2.3 kg/m^2; body fat baseline = 35.3±5.6 %; body fat post = 33.5±5.9 %; VO_{2max} baseline = 32.9±6.6 mL/kg/min; VO_{2max} post = 37.7±5.9 mL/kg/min	12 wk supervised aerobic exercise 5d/wk (500kcal at 75% HR_{max})	Laboratory: Standardized breakfast	Hunger, fullness, PFC and desire to eat (VAS) AG, TG, insulin, insulin sensitivity, GLP-1, PYY over 3h post-breakfast	Reduction in fasting and postprandial insulin post-training. Improvement in insulin sensitivity post-training. Increase in fasting AG after training but no change in postprandial AG. No training effect on TG, GLP-1 and PYY, but tendency for greater GLP-1 AUC in the late postprandial period after training. Increase in fasting hunger, desire to eat and PFC, and decrease in fullness post-training. Greater postprandial hunger and desire to eat post-training.
Martins et al. (2013)	Overweight and obese men and women n =15 (53.3 % men); age = 37±8 years; BMI baseline = 31.3±2.3 kg/m^2; BMI post = 30.1±2.3 kg/m^2; body fat baseline = 35.3±5.6 %; body fat post = 33.5±5.9 %; VO_{2max} baseline = 32.9±6.6 mL/kg/min; VO_{2max} post = 37.7±5.9 mL/kg/min	12 wk supervised aerobic exercise 5d/wk (500kcal at 75% HR_{max})	Laboratory and free-living: 1) Standardized breakfast 2) LE preload 3) HE preload	Hunger, fullness, PFC and desire to eat (VAS) Food intake (1 test meal after preload and food record for remainder of the day) CCK and leptin over 3h post-breakfast	Reduction in fasting and postprandial leptin post-training but no change in CCK. No change in test meal energy intake, but cumulative energy intake after HE preload significantly lower than LE preload post-training, whereas it was greater than LE at baseline. Greater accuracy in energy compensation post-training. No change in macronutrient intake or appetite ratings.

TG, total ghrelin.

Table 2-3 continued

Study	Participants	Training intervention	Setting	Outcome measures	Results
Rosenkilde et al. (2013) Exercise groups	Overweight men Moderate-dose group: n = 18; age = 30±7 years; BMI baseline = 28.6±1.8 kg/m^2; BMI post = 27.5±2.0 kg/m^2; body fat = NR; VO_{2max} baseline = 34.6±24.1 mL/kg/min; VO_{2max} post = 42.3±4.5 mL/kg/min High-dose group: n = 18; age = 28±5 years; BMI baseline = 27.6±1.4 kg/m^2; BMI post = 26.9±1.2 kg/m^2; body fat = NR; VO_{2max} baseline = 36.2±5.3 mL/kg/min; VO_{2max} post = 43.1±6.6 mL/kg/min	12 wk unsupervised daily endurance exercise expending 300kcal/day (moderate-dose) or 600kcal/day (high-dose) at >50%VO_{2max}	Laboratory: 1) Standardized breakfast 2) Exercise test (1h ~60% VO_{2max})	Hunger, satiety, fullness, PFC, palatability and liking (VAS) Food intake (lunch test meal after breakfast) Restraint, disinhibition and susceptibility to hunger (TFEQ) Insulin, PYY_{3-36}, ghrelin post-breakfast	Fasting and postprandial AUC for insulin significantly lower after both exercise interventions. No training effect on PYY_{3-36} or ghrelin. Fasting and postprandial fullness increased in the high-dose group post-intervention. No difference in energy intake, palatability, liking, restraint, disinhibition or susceptibility to hunger within groups.
Shaw et al. (2010) Exercise group	Men n = 13; age = 28±5 years; BMI = NR; body fat baseline = 26.8±1.5 %; body fat post = 23.3±6.3 %; VO_{2max} = NR	8 wk supervised resistance exercise 3d/wk (3 sets 15 repetitions of 9 exercises)	Free-living	Food intake (3-day food record)	No change in energy intake or macronutrient intake with training.

2.3.2.1 Study characteristics: Exercise intervention

The median (range) duration of the interventions was 12 (4-72) weeks of exercise 5 (3-7) d/wk. Exercise duration was prescribed in minutes or energy expenditure (kcal), at intensities in %VO_{2max} or % heart rate maximum (HR_{max}). The median exercise prescription was 43.8 (30-60) min or 500 (300-600) kcal per session at 68.5 (45-90) % VO_{2max} or 70 (70-75) % HR_{max}. Eleven training interventions involved aerobic exercise (Bryant, Caudwell, Hopkins, King, & Blundell, 2012; Caudwell, Finlayson, et al., 2013; Caudwell, Gibbons, Hopkins, King, et al., 2013; Cornier, Melanson, Salzberg, Bechtell, & Tregellas, 2012; Guelfi, Donges, & Duffield, 2013; King et al., 2009; King, Hopkins, Caudwell, Stubbs, & Blundell, 2008; Martins et al., 2010; Martins, Kulseng, Rehfeld, King, & Blundell, 2013; Martins, Truby, & Morgan, 2007; Rosenkilde et al., 2013), two interventions involved resistance exercise (Guelfi et al., 2013; Shaw, Shaw, & Brown, 2010) and one intervention compared moderate intensity interval exercise and high intensity interval exercise in a crossover design (Alkahtani, Byrne, Hills, & King, 2014). One study did not specify the exercise modality (Jakicic et al., 2011). In 11 of the 14 interventions the exercise was supervised (Bryant et al., 2012; Caudwell, Finlayson, et al., 2013; Caudwell, Gibbons, Hopkins, King, et al., 2013; Cornier et al., 2012; Guelfi et al., 2013; King et al., 2009; King et al., 2008; Martins et al., 2010; Martins et al., 2013). Nine studies collected appetite-related measures in a laboratory (Alkahtani et al., 2014; Bryant et al., 2012; Caudwell, Finlayson, et al., 2013; Caudwell, Gibbons, Hopkins, King, et al., 2013; Guelfi et al., 2013; King et al., 2009; King et al., 2008; Martins et al., 2010; Rosenkilde et al., 2013), two studies in free-living conditions (Jakicic et al., 2011; Shaw et al., 2010), and three studies in a combination of laboratory and free-living conditions (Cornier et al., 2012; Martins et al., 2013; Martins, Truby, et al., 2007).

2.3.2.2 Study characteristics: Appetite-related measures

Ten studies included fasting and/or daily (AUC) appetite ratings, all of which included hunger (Alkahtani et al., 2014; Caudwell, Finlayson, et al., 2013; Cornier et al., 2012; Guelfi et al., 2013; King et al., 2009; King et al., 2008; Martins et al., 2010; Martins et al., 2013; Martins, Truby, et al., 2007; Rosenkilde et al., 2013). Fullness (Alkahtani et al., 2014; Caudwell, Gibbons, Hopkins, King, et al., 2013; Guelfi et al., 2013; King et al., 2009; King et al., 2008; Martins et al., 2010; Martins et al., 2013; Martins, Truby, et al., 2007; Rosenkilde et al., 2013), PFC (Cornier et al., 2012; King et al., 2009; King et al., 2008; Martins et al., 2010; Martins et al., 2013; Rosenkilde et al., 2013), desire to eat (Alkahtani et al., 2014; Caudwell, Gibbons, Hopkins, King, et al., 2013; King et al., 2009; King et al., 2008; Martins et al., 2010; Martins et al., 2013), satiety (Cornier et

al., 2012; Rosenkilde et al., 2013), liking and palatability (Martins, Truby, et al., 2007; Rosenkilde et al., 2013) were also assessed. Three studies measured restraint, disinhibition and susceptibility to hunger (Bryant et al., 2012; Cornier et al., 2012; Rosenkilde et al., 2013), one study included the Power of Food Scale, Craving and Mood Questionnaire and Food Craving Inventory (Cornier et al., 2012), one study included the Eating Behaviour Inventory (Jakicic et al., 2011) and one study assessed liking and wanting for foods varying in fat and sweetness (Alkahtani et al., 2014). Eleven studies assessed energy intake, either via a FFQ (Jakicic et al., 2011), food record (Cornier et al., 2012; Shaw et al., 2010), test meals (Alkahtani et al., 2014; Bryant et al., 2012; Caudwell, Finlayson, et al., 2013; Caudwell, Gibbons, Hopkins, King, et al., 2013; King et al., 2008; Rosenkilde et al., 2013), or a combination of test meals and food records (Martins et al., 2013; Martins, Truby, et al., 2007). Two studies measured energy intake following high- and low-energy preloads (Martins et al., 2013; Martins, Truby, et al., 2007) and one at high- and low-energy density meals (Caudwell, Finlayson, et al., 2013). Seven studies reported macronutrient intake (Alkahtani et al., 2014; Cornier et al., 2012; Jakicic et al., 2011; King et al., 2008; Martins et al., 2013; Martins, Truby, et al., 2007; Shaw et al., 2010). Six studies assessed appetite-related peptides in the fasting state (Cornier et al., 2012; Guelfi et al., 2013; Martins et al., 2010; Martins et al., 2013; Martins, Truby, et al., 2007; Rosenkilde et al., 2013) and three in response to food ingestion (Guelfi et al., 2013; Martins et al., 2010; Martins et al., 2013).

2.3.2.3 Participant characteristics

The median (range) age was 38 (28-49) years. The median (range) sample size of the included studies was 18 (10-88). Men and women were included in nine studies, of which the median percentage of men was 33.7 (23.5-53.3) % (Bryant et al., 2012; Caudwell, Finlayson, et al., 2013; Caudwell, Gibbons, Hopkins, King, et al., 2013; Cornier et al., 2012; King et al., 2009; King et al., 2008; Martins et al., 2010; Martins et al., 2013; Martins, Truby, et al., 2007). Four studies only included men (Alkahtani et al., 2014; Guelfi et al., 2013; Rosenkilde et al., 2013; Shaw et al., 2010) and one study only included women (Jakicic et al., 2011).

Nine studies reported BMI before and after the intervention (Bryant et al., 2012; Caudwell, Finlayson, et al., 2013; Caudwell, Gibbons, Hopkins, King, et al., 2013; Guelfi et al., 2013; Jakicic et al., 2011; Martins et al., 2010; Martins et al., 2013; Martins, Truby, et al., 2007; Rosenkilde et al., 2013), the median (range) was 30.5 (22.7-31.8) kg/m^2 at baseline and 30.1 (22.8-31.1) kg/m^2 post-intervention. Seven of these reported a significantly lower BMI after the exercise intervention (Bryant et al.,

2012; Caudwell, Gibbons, Hopkins, King, et al., 2013; Guelfi et al., 2013; Jakicic et al., 2011; Martins et al., 2010; Martins et al., 2013; Rosenkilde et al., 2013). In the four studies that only reported baseline BMI (Alkahtani et al., 2014; Cornier et al., 2012; King et al., 2009; King et al., 2008), the median (range) was 31.8 (30.7-33.3) kg/m^2.

Eight studies reported percent body fat before and after the intervention, the median (range) was 34.3 (23.6-44.1) % at baseline and 32.4 (23.0-42.5) % post-intervention (Bryant et al., 2012; Caudwell, Finlayson, et al., 2013; Caudwell, Gibbons, Hopkins, King, et al., 2013; Jakicic et al., 2011; Martins et al., 2010; Martins et al., 2013; Martins, Truby, et al., 2007; Shaw et al., 2010). Seven of these reported a significantly lower percent body fat after the intervention (Bryant et al., 2012; Caudwell, Finlayson, et al., 2013; Caudwell, Gibbons, Hopkins, King, et al., 2013; Jakicic et al., 2011; Martins et al., 2010; Martins et al., 2013; Shaw et al., 2010). In the three studies that only reported baseline percent body fat, the median (range) was 34.6 (31.2-37.2) % (Alkahtani et al., 2014; Cornier et al., 2012; King et al., 2008).

In the five studies that reported VO_{2max} before and after the intervention, the median (range) was 32.9 (29.1-36.2) mL/kg/min at baseline and 37.7 (34.3-43.3) mL/kg/min post-intervention (Caudwell, Gibbons, Hopkins, King, et al., 2013; Martins et al., 2010; Martins et al., 2013; Martins, Truby, et al., 2007; Rosenkilde et al., 2013). In all studies, the increase in VO_{2max} with training was significant. In the four studies that only reported baseline VO_{2max}, the median (range) was 28.8 (28.4-29.1) mL/kg/min (Alkahtani et al., 2014; Bryant et al., 2012; King et al., 2009; King et al., 2008).

2.3.2.4 Study results: Appetite ratings

Exercise training led to differences in appetite ratings in five of 10 studies. Three studies found an increase in fasting hunger (Caudwell, Gibbons, Hopkins, King, et al., 2013; King et al., 2009; Martins et al., 2010), desire to eat and PFC (Martins et al., 2010), and a decrease in fullness (Martins et al., 2010). However, two studies found that fasting fullness increased following aerobic (Guelfi et al., 2013) and high-dose aerobic (600kcal/d) (Rosenkilde et al., 2013) exercise training. King et al. (2009) reported a greater daily hunger, desire to eat and lower fullness post-training in a subsample of non-responders to exercise-induced weight loss (i.e. individuals with changes in body composition below that expected based on the total exercise-induced energy expenditure). In response to a standardized breakfast, Martins et al. (2010) found an increase in hunger and desire to eat following exercise training, whereas Guelfi et al. (2013) found an increase in fullness after an oral glucose tolerance test following aerobic training.

The two studies that included SQ found increases post-training (Caudwell, Gibbons, Hopkins, King, et al., 2013; King et al., 2009). Only one of three studies found a reduction in disinhibition and an increase in restraint post-training (Bryant et al., 2012).

2.3.2.5 Study results: Energy and macronutrient intake

Five of 11 studies found differences in energy intake after the exercise-training interventions. Daily energy intake was lower post-training in one study (Cornier et al., 2012), while it increased in a subsample of compensators in another study (King et al., 2008). As for high-energy test meal challenges, Caudwell et al. (2013) showed a reduction in meal size containing high energy density foods, and two studies demonstrated that energy intake was lower throughout the day after a high-energy preload compared to a low-energy preload (Martins et al., 2013; Martins, Truby, et al., 2007).

Two studies showed an increase in percent energy from fat in subsample of compensators (individuals whose weight loss after exercise-training was less than predicted based on the total exercise-induced energy expenditure) (King et al., 2008) or after moderate-intensity interval training (Alkahtani et al., 2014). Training led to an increase in percentage energy from protein in another study (Martins, Truby, et al., 2007).

2.3.2.6 Study results: Appetite-related peptides

Of the studies that assessed fasting peptides, five found differences following exercise training, where leptin (Cornier et al., 2012; Guelfi et al., 2013; Martins et al., 2013) and insulin decreased (Martins et al., 2010; Rosenkilde et al., 2013), and ghrelin increased (Martins et al., 2010). Insulin sensitivity improved after training in two of three studies (Guelfi et al., 2013; Martins et al., 2010). Of note, the study that found no improvement in insulin sensitivity was half the duration of the two others (6 vs. 12 weeks) (Martins, Truby, et al., 2007). All three studies that assessed the peptide response to food ingestion found training effects, where postprandial leptin (Guelfi et al., 2013; Martins et al., 2013) and insulin decreased (Guelfi et al., 2013; Martins et al., 2010) after aerobic training while there was a tendency for GLP-1 in the late postprandial period to increase with training (Martins et al., 2010).

2.4 Discussion

2.4.1 Appetite control in active and inactive individuals

This systematic review investigated differences in appetite ratings, food intake and appetite-related peptides between active and inactive (or previously inactive) individuals in order to determine whether habitual physical activity improves appetite control. In terms of fasting, postprandial or daily appetite ratings, studies reported mixed results such that no clear differences could be distinguished between physically active and inactive individuals. It has been suggested that combining appetite sensations with objectively measured energy intake to calculate parameters such as the SQ can provide a better indication of the ability of the energy consumed to affect appetite. One cross-sectional study (Harrington et al., 2013) and two exercise-training studies (Caudwell, Gibbons, Hopkins, King, et al., 2013; King et al., 2009) assessed SQ with conflicting results, however the former measured SQ during an ad libitum meal while in the latter studies SQ was measured during a standardized meal. These differences, along with differences in the protocols in the other studies, may account for the contradictory results in appetite ratings.

Several studies focused on the measurement of energy intake, but no consistent differences were again found between active and inactive individuals. However, these simple comparisons precluded the possibility that physical inactivity may lead to the dysregulation of appetite and subsequent overconsumption, meaning that differences between active and inactive individuals may not always be apparent. Indeed, Blundell (2011) has argued that the relationship between physical activity and energy intake may follow a curvilinear function. After transforming absolute energy intake into standardized scores and distinguishing levels of physical activity from the definitions of the ‘active’ groups used in the cross-sectional studies, this hypothesis could be tested. The results revealed a significant quadratic effect illustrated by a J-shaped curve across physical activity levels (see Figure 2-2). A similar J-shaped relationship has recently been suggested by Shook et al. (2015), who compared estimated energy intake, using an equation based on changes in body composition, across quintiles of physical activity in a large heterogeneous sample of young adults. Their analysis provides further support to the current synthesis of the literature which demonstrates that the relationship between physical activity level and energy intake is non-linear, as postulated over 60 years ago and described in Chapter 1 (Mayer et al., 1956). This relationship may explain why differences in energy intake may not be obvious between active and inactive individuals as they may be situated at similar levels on the energy intake curve. As these findings are based on standardized scores from results of studies using various methodologies and protocols (Apolzan et al.,

2009; Catenacci et al., 2014; Charlot & Chapelot, 2013; Harrington et al., 2013; Jago et al., 2005; Jokisch et al., 2012; Lund et al., 2013; Rocha et al., 2013, 2015; Van Walleghen et al., 2007) or inferred from changes in body composition (Shook et al., 2015), confirmation of this J-shaped relationship is required with objective measures of energy intake in studies designed to assess intake across well-defined physical activity levels.

Of interest to this review are the studies that used preload challenges or macronutrient manipulations to examine whether differences exist in the ability to adjust energy intake after previous food intake or in meals that vary in macronutrient composition. Three studies demonstrated that physically active individuals have a better ability to make adjustments in energy intake following a high-energy preload (Long et al., 2002; Martins et al., 2013; Martins, Truby, et al., 2007), suggesting an increased sensitivity to previous energy intake (e.g. enhanced satiety). Another preload study also found more accurate energy compensation in active individuals, where the no preload condition led to an increase in energy intake in active but not inactive individuals (Van Walleghen et al., 2007). In line with these studies, one study found that exercise training led to a reduction in meal size at a high-energy dense meal but not at a low-energy dense meal (Caudwell, Finlayson, et al., 2013). This also supports the proposition of increased sensitivity to the energy density of foods, but this time during a meal (e.g. enhanced satiation). Interestingly, in this study it appeared that women may have been more susceptible to the effect than men. Therefore, further studies in males and females are required to confirm this finding and the potential interaction between physical activity and energy density on the sensitivity of appetite control. Nonetheless, these data support a J-shaped relationship between physical activity and energy intake, and suggest a better ability to regulate energy intake with increasing levels of physical activity.

Despite the effects observed following a preload, there was no consistent effect of physical activity level on energy compensation immediately after an exercise bout or over several hours or days after exercise (Alkahtani et al., 2014; Charlot & Chapelot, 2013; Jokisch et al., 2012; Rocha et al., 2013, 2015). These results do not support a recent meta-analysis that found that absolute energy intake after acute exercise was greater in active individuals compared to those less active (Schubert et al., 2013). However, this analysis only reported absolute energy intake and not energy compensation. In fact, Charlot & Chapelot (2013) report in their study on lean/fit and fat/unfit men that energy compensation after exercise was highly variable and found no clear differences between groups. This raises the concern of the reliability of the measure of energy compensation (discussed in Section 2.4.3). Nevertheless, in the acute/short-term it appears that in physically active individuals, compensatory

responses in energy intake may be more sensitive to previous food intake than exercise.

2.4.2 Differences in the proposed mechanisms of appetite control

Eating behaviour is influenced by several proposed mechanisms, one of which is appetite-related peptides. Acute exercise and exercise training also affect these peptides (Schubert et al., 2014; Stensel, 2010). The studies that measured the peptide response to food intake found lower postprandial insulin (Guelfi et al., 2013; Lund et al., 2013; Martins et al., 2010; Rosenkilde et al., 2013) and greater postprandial GLP-1 (Lund et al., 2013) (and tendency (Martins et al., 2010)) in active individuals. An emphasis on insulin will be considered as it was the most commonly measured hormone in the studies within the review. Interestingly, the same subjects that showed a preload effect in the study by Martins et al. (2013) also showed an improvement in insulin sensitivity (Martins et al., 2010). Additionally, the aerobic training group in the study by Guelfi et al. (2013) significantly lowered postprandial insulin and improved insulin sensitivity with concomitant changes in postprandial fullness. However, the resistance-training group in the same study had a tendency for lower postprandial insulin (p=.066) and also improved insulin sensitivity after training without an effect on postprandial appetite ratings, while another study that showed a preload effect after six weeks of training did not find a significant improvement in insulin sensitivity (Martins, Truby, et al., 2007). Despite the relationship between insulin and appetite control not being consistent in the above studies, a meta-analysis from Flint et al. (2007) proposed that insulin resistance could lead to disrupted satiety signalling. This meta-analysis showed that postprandial insulin was associated with satiety in individuals with a healthy weight but not in overweight individuals; however it did not take into account physical activity status of the participants nor their body composition (fat mass and fat-free mass).

Measuring body composition, rather than just BMI, has become important in understanding the mechanisms affecting eating behaviour as fat-free mass (but not fat mass) was found to be associated with daily energy intake and meal size in overweight and obese individuals (Blundell et al., 2012a). In addition to appetite signals from adipose tissue and gut peptides, Blundell et al. (2012b) proposed a role for fat-free mass and resting metabolic rate as drivers of food intake. Differences in body composition were apparent in the cross-sectional studies, as six reported lower body fat percentage in active individuals (Apolzan et al., 2009; Jokisch et al., 2012; Lund et al., 2013; Rocha et al., 2013, 2015; Van Walleghen et al., 2007) despite only two reporting a lower BMI (Apolzan et al., 2009; Rocha et al., 2013). Three of the former studies reported enhanced appetite control in terms of more accurate energy

compensation (Jokisch et al., 2012; Rocha et al., 2013; Van Walleghen et al., 2007). No cross-sectional studies compared lean and overweight active individuals, thus a question arises as whether 'fat but fit' individuals would have enhanced appetite control. Four training studies conducted in overweight participants reported improvements in appetite control post-intervention (but also showed significant reductions in fat mass) (Caudwell, Finlayson, et al., 2013; Caudwell, Gibbons, Hopkins, King, et al., 2013; Guelfi et al., 2013; Martins et al., 2013). Overall, these studies indicate that differences in body composition and insulin sensitivity may be factors promoting more sensitive appetite control in active individuals. Furthermore, Horner et al. (2015) found faster gastric emptying in active compared to inactive males, proposing another mechanism by which appetite control (i.e. satiety signalling) could be better regulated in physically active individuals. More studies are required to elucidate the mechanisms involved in the appetite control differences between active and inactive individuals such as body composition, postprandial satiety and hunger peptides, insulin (and possibly leptin (Dyck, 2005; Steinberg et al., 2004)) sensitivity, gastric emptying in addition to resting metabolic rate (Blundell, Finlayson, et al., 2015; Caudwell, Finlayson, et al., 2013) and substrate oxidation (Hopkins, Jeukendrup, King, & Blundell, 2011), which were not covered in this review.

2.4.3 Methodological considerations

A number of points regarding the methodologies used in the studies included in this review need addressing. In the cross-sectional studies, the definitions used to define active and inactive individuals varied markedly. For example, some studies only used a self-rated measure such as a 'yes or no' question (Georgiou et al., 1996) or Likert scale (Deshmukh-Taskar et al., 2007; Gregersen et al., 2011; Jago et al., 2005) or a self-reported measure such as physical activity questionnaires (Catenacci et al., 2014; Van Walleghen et al., 2007) or diaries/recalls (Jokisch et al., 2012; Long et al., 2002) instead of objectively assessing physical activity via accelerometry. This may have confounded the results of the active groups from participants overestimating their physical activity habits (Dhurandhar et al., 2014; Sallis & Saelens, 2000). Moreover, some studies only used VO_{2max} (Charlot & Chapelot, 2013; Lund et al., 2013) to define the active groups, which may not reflect all aspects of physical activity (e.g. low- to moderate-intensity activity) (Jacobs, Ainsworth, Hartman, & Leon, 1993). Clear definitions of activity levels should be set in place to allow future studies to investigate appetite and energy intake across these defined levels. Along these lines, the studies in this review preclude the distinction of the effects of the several components of physical activity, such as time spent in low, moderate and vigorous activities, cardiorespiratory fitness and PAEE, on appetite control. In addition, future studies

should assess all components of energy intake and energy expenditure in order to determine their influence on eating behaviour, particularly in light of recent evidence suggesting a plateau in daily energy expenditure above a certain threshold of physical activity (Pontzer et al., 2016). This would help to tease out whether changes in cardiorespiratory fitness and/or PAEE are important for appetite control.

Secondly, food intake was assessed both in laboratory (using test meals) and in free-living conditions (using FFQ and food diaries). Test meals are known to be a rigorous method of assessing energy intake (under controlled laboratory conditions) but food diaries, despite providing a longer window of observation of 'real world' feeding patterns, may lead to underreporting and biased results (Dhurandhar et al., 2014). It should be noted that the short-term results (daily energy intake) observed in the preload studies were based on food diaries (Long et al., 2002; Martins et al., 2013; Martins, Truby, et al., 2007; Van Walleghen et al., 2007). These data should be replicated in more rigorous conditions to confirm the observed effects.

Thirdly, the within-subject (i.e. test re-test reliability) and between-subject (i.e. inter-individual variability) consistency in energy compensation following preload intake is often not acknowledged in studies, and this should be addressed in light of recent studies demonstrating marked inter-individual variability (Charlot & Chapelot, 2013; Finlayson, Bryant, Blundell, & King, 2009; Hopkins, Blundell, & King, 2014; Unick et al., 2010) and modest test re-test reliability (Unick et al., 2015) in energy compensation following acute exercise. The composition of the preloads and tests meals should also be further examined to determine whether physical activity enhances the sensitivity to energy density or to specific macronutrients.

Finally, the sample size in most of the studies was small, which may have resulted in non-significant results and overlooked relatively small but important effects. The studies were also not designed to test effects of sex, body composition (lean vs. overweight/obese), and exercise mode; therefore this does not allow for the determination of specific criteria or characteristics eliciting the reported effects (or lack thereof).

2.4.4 Review limitations

This review included a limited number of studies assessing a broad range of appetite-related measures between active and inactive individuals using various definitions. This may have led to some of the inconsistent patterns or lack of effects observed. Physical activity encompasses not only exercise training but also activities of daily living, and as most definitions were based on a minimal level of moderate-intensity structured exercise, the studies included in this review lean towards a comparison

between exercise-trained and untrained individuals. Therefore, these results should be interpreted with caution while more studies assessing all facets of habitual physical activity become available. Clearly, there is a lot more work to be done to elucidate the effects of physical activity and exercise on the appetite control system.

2.5 Conclusions

It can be concluded from this review that habitually active individuals appear to have increased ability to compensate to changes in the energy content/density of foods compared to inactive individuals despite showing no group differences in subjective appetite ratings. This review also supports the formulation that the relationship between physical activity level and energy intake may be non-linear, as reflected by the J-shaped curve obtained from analysis of standardized energy intake scores across studies. The mechanisms underlying this effect are not known but could include differences in body composition (fat mass and fat-free mass), postprandial hunger or satiety peptides, or sensitivity to tonic peptides such as insulin or leptin. This characteristic of active individuals could mitigate the risk of overconsumption in an energy-dense food environment. Further studies are required to confirm these findings.

Chapter 3 – General methods

3.1 Ethical considerations

Ethical approval was obtained by the School of Psychology Ethical Committee for the studies in Chapters 4 to 6 (15-0181, 15-0382) and from the Leeds West NHS Research Ethics Committee for the study in Chapter 7 (09/H1307/7). All participants provided written informed consent prior to taking part. The main procedures of the studies were explained prior to obtaining consent, but to avoid impacting eating behaviour, the specific objectives were not fully disclosed to the participants until after study completion. At this time, the participants were then fully debriefed about the true purpose of the study and given the opportunity to ask questions.

3.1.1 Participant recruitment and screening

Participants were recruited from the University of Leeds (Leeds, UK) and surrounding area via poster advertisements and mailing lists. Interested participants were provided with a participant information sheet, and if they were still interested in participating in the study they were invited to complete an online screening questionnaire to assess eligibility, which included questions pertaining to medical, diet and physical activity history, food allergies and intolerances, and food preferences. Participants required to be non-smoker, weight stable (±2 kg for previous 3 months), not currently dieting, have no history of eating disorders, not taking any medication known to affect metabolism or appetite, and acceptance of the study foods. Further eligibility criteria specific to the studies are explained within each experimental chapter.

3.2 Scientific approach: Multi-level experimental platform

This thesis investigates the role of physical activity level in appetite control using a multi-level experimental platform assessing several dimensions of appetite control as shown in Figure 3-1 – environmental, behavioural, psychological, physiological, and metabolic (Caudwell et al., 2011). This was achieved with objective measures of energy balance (physical activity, energy expenditure and energy intake) and rigorous biopsychological methodology that included appetite sensations, body composition, resting metabolic rate, cardiorespiratory fitness, appetite-related peptides, eating behaviour traits, and food reward. These are explained in the sections below.

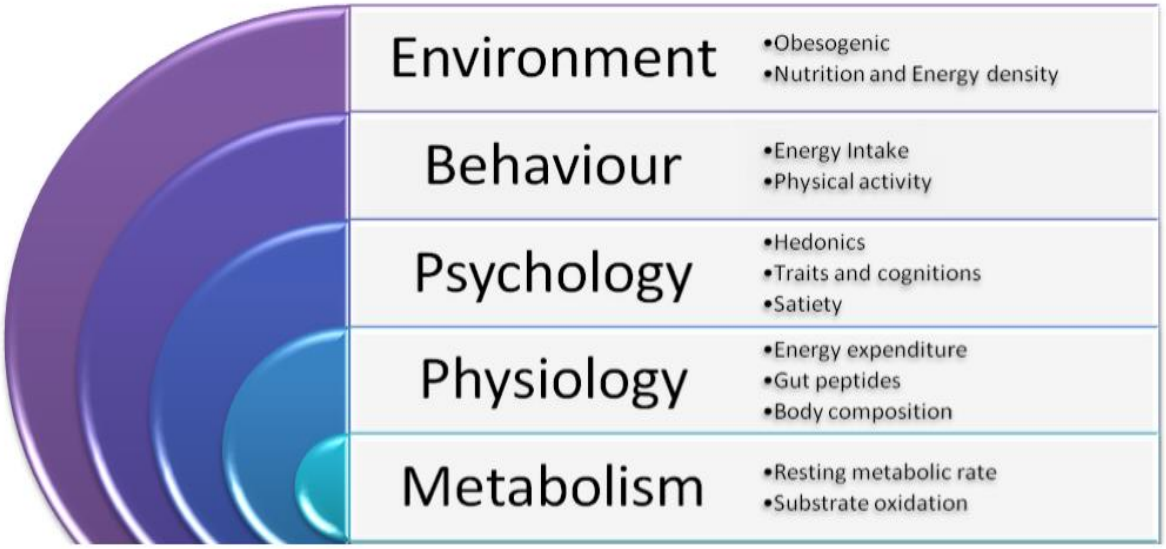

Figure 3-1 Schematic of the Leeds multi-level experimental platform assessing appetite control

3.3 Behavioural measurements

3.3.1 Energy intake

Throughout this thesis, energy intake was determined using laboratory-based test meals. Details of the meals and procedures from each study are described further in each experimental chapter. All test meals were served in separate feeding cubicles free from distractions within the Human Appetite Research Unit, School of Psychology, University of Leeds (UK). During ad libitum meals, which provided food in excess of expected consumption, the participants were instructed to eat as little or as much as they desired until comfortably full. During the fixed energy meals, the participants were instructed to eat all the food and drink provided. All food and drinks were weighed before and after consumption to the nearest 0.1 g and macronutrient intake were calculated from the manufacturers' food labels. Energy intake was subsequently calculated using energy equivalents for protein, fat and carbohydrate of 4, 9 and 3.75 kcal/g, respectively. Liking of the study foods was assessed within the screening questionnaires prior to study commencement, with individuals not eligible to participate if they strongly disliked any of the study foods.

3.3.2 Physical activity

3.3.2.1 Physical activity questionnaire

The short-form of International Physical Activity Questionnaire (IPAQ; Craig et al., 2003) was integrated within the screening questionnaire prior to study commencement in Chapters 4 and 5 to assess habitual physical activity in order to distribute participants evenly among physical activity levels (e.g. low, moderate and high). Specific participant groupings are explained further in the experimental chapters. The short-form of the IPAQ comprises of four sets of questions asking about the physical activities performed in the previous seven days. The questions pertain to the number of days per week and hours or minutes per day spent doing vigorous activities, moderate activities, walking and sitting. The IPAQ has been shown to have good reliability and validity (Craig et al., 2003). However, as self-reported measures of physical activity may not provide accurate information (Sallis & Saelens, 2000), a physical activity monitor (SenseWear Armband, described below) was used as an objective measure of physical activity once the participants were included in the studies.

3.3.2.2 Physical activity monitor

In Chapters 4 to 6, participants wore the SenseWear Armband (SWA; BodyMedia, Inc., Pittsburgh, USA) to measure 7-day habitual physical activity and sedentary behaviour, as shown in Figure 3-2.

Figure 3-2 SenseWear Armband

Participants were instructed to wear the SWA on their non-dominant arm over seven days for at least 23 hours per day (awake and asleep, except for the time around showering, bathing or swimming). Compliance was defined as five days of wear (including one weekend day) with at least 22 h of verifiable time per day. The SWA measures minute-by-minute tri-axial accelerometry, galvanic skin response, skin temperature and heat flux (Figure 3-3). Proprietary algorithms available in the accompanying software (version 8.0 professional) calculate TDEE, and minutes spent

sleeping, sedentary and in light, moderate and vigorous physical activity. Physical activities were classified into light (1.5-2.9 METs), moderate (3.0-5.9 METs) and vigorous (≥ 6.0 METs). Physical activity level (PAL; TDEE/basal metabolic rate) for each participant was calculated by the software using basal metabolic rate obtained from the WHO equation (World Health Organization, 2004). A PAL between 1.40-1.69 was classified as inactive to light activity lifestyle and a PAL between 1.70-1.99 as an active to moderately active lifestyle (World Health Organization, 2004). The SWA has shown good accuracy in estimating free-living TDEE and various intensities of physical activity (Johannsen et al., 2010; St-Onge, Mignault, Allison, & Rabasa-Lhoret, 2007; Welk, McClain, Eisenmann, & Wickel, 2007).

Figure 3-3 Sensors of the SenseWear Armband

3.4 Psychological measurements

3.4.1 Hedonics and food reward

The Leeds Food Preference Questionnaire (LFPQ) was administered to determine scores of implicit wanting and explicit liking for high-fat and low-fat foods matched for familiarity, sweetness, protein, and acceptability (Figure 3-4; Finlayson, King, & Blundell, 2008). Prior to the procedure, screening of the photographs used in the task was completed by each participant to improve internal validity. If a participant did not know, recognise or would never/rarely eat a particular food item used in the study, replacement photographs were chosen from a database of images of similar composition. The LFPQ has been validated in a wide range of research (Finlayson, Arlotti, Dalton, King, & Blundell, 2011; Griffioen-Roose, Finlayson, Mars, Blundell, & de Graaf, 2010; Verschoor, Finlayson, Blundell, Markus, & King, 2010). The LFPQ is used in throughout the thesis as a measure of hedonic preference in liking and wanting for high-fat relative to low-fat foods. Table 3-1 shows the nutritional characteristics of the food images used.

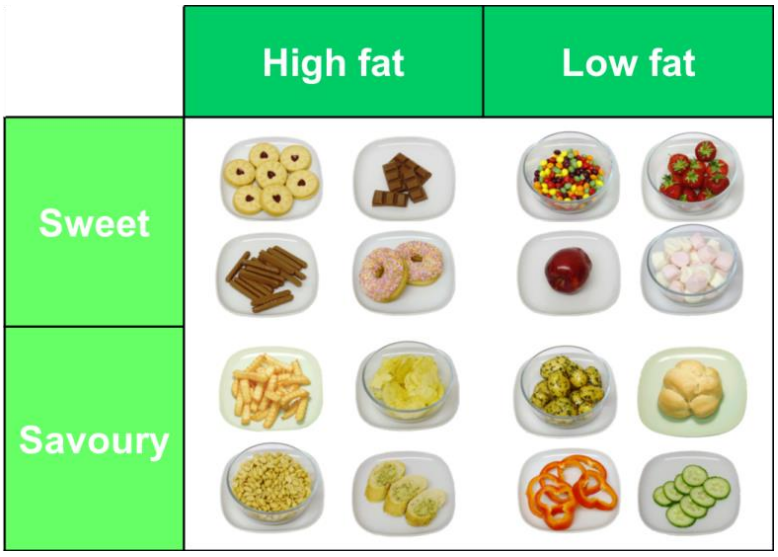

Figure 3-4 Food array used in the LFPQ

Table 3-1 Nutritional characteristics of the high-fat and low-fat food images used in the LFPQ

High-fat	% CHO	% protein	% fat	kcal/ 100g	Low-fat	% CHO	% protein	% fat	kcal/ 100g
Jam biscuits	60.0	4.6	30.7	440	Skittles	83.1	0.0	9.4	403
Chocolate	40.2	5.7	51.1	525	Strawberries	74.0	10.7	3.0	30
Chocolate fingers	39.2	4.7	42.3	575	Apple	82.4	3.0	1.7	53
Doughnut	43.3	6.7	46.5	410	Marshmallows	71.9	3.2	0.0	498
Chips	47.2	5.4	46.7	239	Potatoes	80.6	10.6	2.3	79
Crisps	34.2	4.4	57.2	537	Bread roll	58.9	18.5	12.5	245
Salted peanuts	6.3	18.7	74.8	590	Red peppers	74.0	12.5	11.3	32
Garlic bread	37.9	7.9	47.7	345	Cucumber	52.9	15.2	12.7	21
Mean	**38.5**	**7.2**	**49.6**	**458**	**Mean**	**72.2**	**9.2**	**6.6**	**170**

Implicit wanting (Figure 3-5) was assessed by asking the participants to select as fast as possible which food from specific categories “they most want to eat”. Scores for implicit wanting were computed from mean response times adjusted for frequency. To calculate wanting fat appeal bias as a measure of hedonic preference for high-fat foods, low-fat scores were subtracted from high-fat scores, thus a positive score indicates greater implicit wanting towards high-fat compared to low-fat foods.

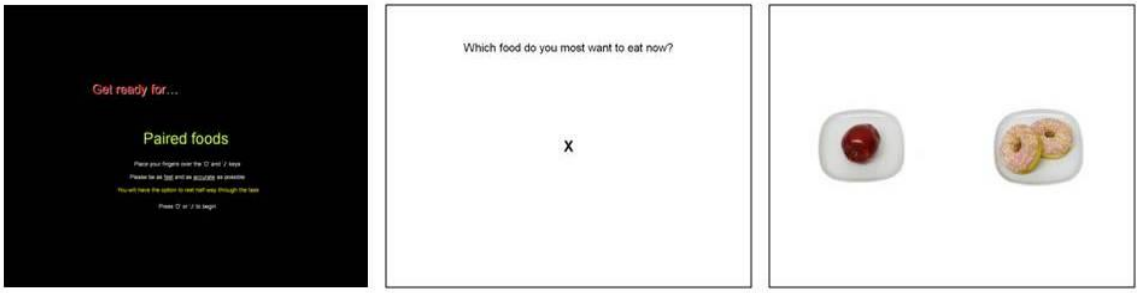

Figure 3-5 Representation of the implicit wanting and food choice trials in the LFPQ

To measure explicit liking (Figure 3-6a), the participant rated the extent to which they liked each food (How pleasant would it be to taste this food now?). The food images were presented individually, in a randomised order and participants made their ratings using a 100-mm visual analogue scale (VAS). Explicit wanting (Figure 3-6b) was assessed in a similar manner, in response to the extent to which they want each food “How much do you want some of this food now?” To calculate fat appeal bias as a measure for hedonic preference for high-fat foods, low-fat scores were subtracted from high-fat scores, thus a positive score indicates greater explicit liking or wanting towards high-fat compared to low-fat foods.

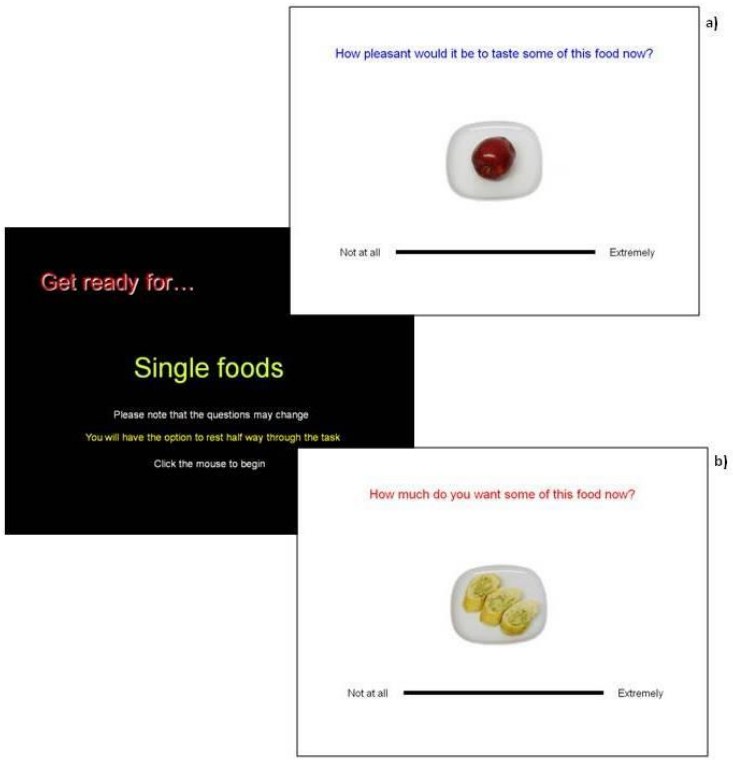

Figure 3-6 Representation of the explicit liking (a) and explicit wanting (b) trials

3.4.2 Eating behaviour traits

3.4.2.1 Three Factor Eating Questionnaire

The Three Factor Eating Questionnaire (TFEQ; Stunkard & Messick, 1985) is a validated 51-item instrument that measures three dimensions of eating behaviour: cognitive control of restraint (i.e. concern over weight gain and the strategies adopted to prevent this), disinhibition of eating (i.e. tendency of an individual to overeat and to eat opportunistically in the obesogenic environment), and susceptibility to hunger (i.e. extent to which feelings of hunger are perceived and how these sensations result in food intake). Participants respond true or false to the first 36 items, then chose one of four possible responses for the remaining 15 items, reflecting their level of agreement with a particular statement. Responses are scored for each of the three factors so that a higher score reflects a greater level of eating disturbances.

3.4.2.2 Binge Eating Scale

The Binge Eating Scale (BES; Gormally et al., 1982) is a validated 16-item questionnaire that assesses the severity of binge eating. The questions are based on both behavioural characteristics (e.g. amount of food consumed) and emotional/cognitive responses (e.g. guilt or shame). The total score ranges from 0 to 46, with the highest score denoting severe binge eating behaviour.

3.4.2.3 Control of Eating Questionnaire

The Control of Eating Questionnaire (CoEQ; Hill et al., 1991) is validated and comprised of 21 items that are designed to assess the severity and type of food cravings experienced over the previous seven days. The CoEQ has four subscales assessed by 100-mm VAS; Craving Control, Craving for Sweet Foods, Craving for Savoury Foods and Positive Mood (Dalton, Finlayson, Hill, & Blundell, 2015).

3.4.3 Subjective appetite sensations and satiety

Appetite ratings were assessed via VAS for hunger, fullness, desire to eat and prospective food consumption. VAS for the measurement of appetite sensations have been shown to be valid and reproducible (Flint, Raben, Blundell, & Astrup, 2000). Each of the following questions “How hungry do you feel now?”; “How full do you feel now?”; “How strong is your desire to eat now?”; “How much food do you think you could eat?” were answered on an horizontal line anchored at each end by the words “Not at all” and “Extremely”. Ratings ranged between 0-100. Pen and paper VAS were used to assess appetite ratings in Chapter 4, whereas a validated hand-held Electronic Appetite Rating System shown in Figure 3-7 (Gibbons, Caudwell, Finlayson, King, & Blundell, 2011) was used in Chapters 5 and 7. It has previously been shown that pen and paper VAS and the specific electronic appetite rating system used in this thesis show good agreement (Gibbons et al., 2011). Area under the curve (AUC) was calculated using the trapezoid rule (Matthews, Altman, Campbell, & Royston, 1990).

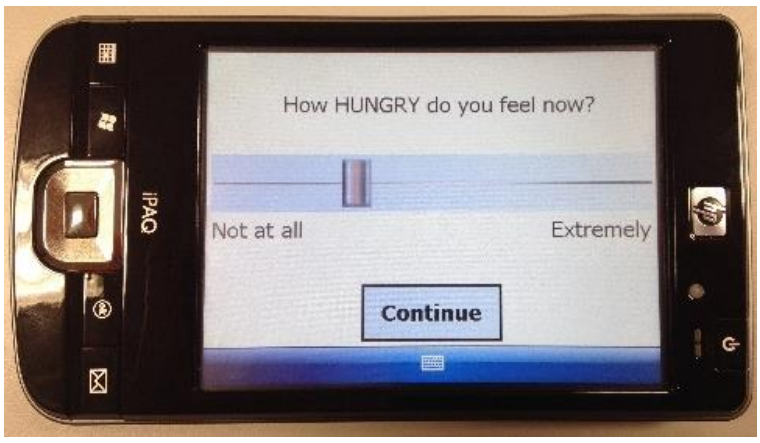

Figure 3-7 Electronic Appetite Rating System to assess subjective appetite sensations

3.4.3.1 Satiety quotient

The satiety quotient (SQ) measures the satiating effect of food in relation to the changes in ratings of hunger before and following a meal. The SQ has been previously validated (Drapeau et al., 2007; Green, Delargy, Joanes, & Blundell, 1997) as a predictor of energy intake and is calculated using the following formula:

$$SQ\ (mm/kcal) = \frac{(\text{rating before eating episode} - \text{rating after eating episode})}{\text{Energy of the food consumed}} \times 100$$

3.5 Physiological measurements

3.5.1 Energy expenditure

As described in Section 3.3.2.2, objectively-measured TDEE was obtained from the SWA. In Chapter 6, PAEE was calculated by subtracting measured RMR (see Section 3.6.1) and estimated thermic effect of food (~10% of TDEE) following the equation PAEE = 0.9TDEE – RMR (Westerterp, 2004).

3.5.2 Appetite-related peptides

To further assess the contribution of physical activity in the homeostatic control of appetite, fasted appetite-related peptides were measured in Chapters 4 and 7. In Chapter 4, these included leptin, acylated ghrelin, insulin and glucose, and in Chapter 7, leptin, total ghrelin, insulin, glucose, GLP-1 and PYY. Blood collection and analyses specific to the studies are explained within each experimental chapter.

3.5.3 Body composition

Anthropometric and body composition measures were taken whilst participants were wearing tight fitting clothing (swimwear, lycra/compression shorts, sports bra) and a swim cap. Standing height without shoes was measured to the nearest 0.1 cm using a stadiometer (Leicester height measure, SECA, UK). Body mass was measured using an electronic balance and recorded to the nearest 0.1 kg. Body mass index (BMI) was calculated from the following equation:

$$BMI\ (kg/m^2) = \text{body mass}/\ \text{height}^2$$

Waist circumference was measured to the nearest 0.1 cm using a measuring tape at the level just above the umbilicus (i.e. narrowest point). Fat mass, fat-free mass and percentage body fat were estimated via air displacement plethysmography (BodPod,

Life Measurement, Inc., Concord, USA) following the manufacturer's instructions and using the Siri equation (Siri, 1961):

$$\text{Body fat (\%)} = (4.95 / \text{body density} - 4.5) \times 100$$
$$\text{Body density (kg/m}^3\text{)} = \text{body mass / body volume}$$

3.5.4 Cardiorespiratory fitness

Cardiorespiratory fitness (VO_{2max}) was determined in Chapters 4-6 using a maximal incremental treadmill test based on the modified Balke protocol (American College of Sports Medicine, 2010). The incline increased 2% in the first minute of the test and 1% for each additional minute, until volitional exhaustion. Expired gases (Vyntus CPX, CareFusion; UK) and heart rate (Polar RS400, Polar; Finland) were measured continuously during the test. Prior to each test, the gas analyser was calibrated using gases of known concentrations while the volume sensor was calibrated automatically by the system at flow values of 2 L/s and 0.2 L/s. Ratings of perceived exertion were collected at the end of each minute using the Borg scale (Borg, 1998). The average of the last 20 seconds of the test was considered VO_{2max}. A true VO_{2max} was characterised by attainment of at least two of the following criteria: a plateau (≤2mL/kg/min) in VO_2 with an increase in workload, an RER of ≥1.05 and a heart rate ≥90% of age-predicted maximum heart rate (220-age) (Achten & Jeukendrup, 2003).

In Chapter 7, VO_{2max} was determined using a two-phase incremental treadmill test to volitional exhaustion (Achten & Jeukendrup, 2003) with expired gases (Sensormedics Vmax29, Yorba Linda, USA) and heart rate measured continuously as described above. Participants walked on the treadmill at a speed of 3.5 km/h at a 1% incline with the speed increasing by 1 km/h every 3 minutes until the speed reached 6.5 km/h. After this point, the incline was increased by 2% every 3 minutes until attainment of an RER of >1.0. Then the speed was increased by 1 km/h every minute until volitional exhaustion. The average of the last 20 seconds of the test was considered VO_{2max}. Attainment of true VO_{2max} was characterised with the same criteria as above.

3.6 Metabolic measurements

3.6.1 Resting metabolic rate and substrate oxidation

Resting metabolic rate (RMR) was measured with an indirect calorimeter fitted with a ventilated hood (GEM; Nutren Technology Ltd) following the guidelines of The American Dietetic Association (Compher, Frankenfield, Keim, & Roth-Yousey, 2006).

Participants were required to remain awake but motionless in a supine position for 40 minutes. The average of the last 30 minutes of collection was used to determine RMR. VO_2 and VCO_2 were calculated from O_2 and CO_2 concentrations in inspired and expired air diluted in a constant airflow of ~40 L/min (individually calibrated for each participant) and averaged over 30-second intervals. Substrate oxidation (respiratory exchange ratio; RER) was calculated by the software using standard stoichiometric equations (e.g. Peronnet & Massicotte, 1991).

3.7 Statistical approach

Data are reported as mean ± standard deviation throughout, with figures reporting mean ± standard error of the mean. IBM SPSS for Windows (version 21; USA) was used for statistical analyses. Data were visually inspected for normality and outliers prior to statistical treatment using histograms and boxplots, respectively. ANOVA was the primary method of analysis to investigate the effect of physical activity level (Chapters 4 and 5: between-subject factor) or exercise training (Chapter 7: within-subject factor) on the response to the dietary manipulations (within-subject factor). Where appropriate, Greenhouse-Geisser probability levels were used to adjust for non-sphericity, and post hoc analyses were performed using the Bonferroni adjustment for multiple comparisons. Further specific statistical procedures are explained in more detail within the methods section of each experimental chapter. Statistical significance was established at $p<.05$.

Chapter 4 – Impact of physical activity level on the acute satiation response to passive overconsumption (COMPAS – overCOnsuMption and Physical Activity Status)

Chapter aim:

- Assess the effects of physical activity level on satiation, passive overconsumption and food reward in response to meals varying in dietary fat content in lean individuals.

4.1 Introduction

There is abundant evidence to support the benefits of habitual physical activity in weight management (Donnelly et al., 2009). Myers et al. (2017) have recently shown significant negative associations between objectively-measured MVPA and markers of adiposity. On the other side of the energy balance, the contribution of high-fat energy-dense foods towards obesity cannot be ignored (Mendoza, Drewnowski, & Christakis, 2007; Vernarelli, Mitchell, Rolls, & Hartman, 2015). Passive overconsumption is a global phenomenon and originates from changes in the food supply towards increasingly energy-dense foods, contributing greatly to the obesity epidemic (Swinburn et al., 2011). This is reflected by an unintentional increase in energy intake, arising from a failure to appropriately adjust intake in response to energy density (Blundell & MacDiarmid, 1997).

Control over food intake is strongly influenced by ingestive and post-ingestive feedback from satiation and satiety, two separate aspects of appetite that inhibit eating (Blundell et al., 2010). Satiation is the process that terminates feeding, measured by the amount of food eaten at a meal, and satiety is the process involved in post-meal suppression of hunger (Blundell et al., 2010). Satiety can be measured in a variety of ways, and is often measured with a preload-test meal paradigm using preloads differing in energy content (Blundell et al., 2010). The SQ, calculated from changes in appetite scores relative to a meal's energy content (Green et al., 1997), can also provide a measure of satiation (immediately after food consumption) and satiety (over a specified amount of time after food consumption) (King et al., 2009). Dietary fat exerts a weaker effect on satiation within a meal than carbohydrate or protein, and is a key driver of passive overconsumption (Blundell & MacDiarmid, 1997). For example, in the short-term, when eating ad libitum and to a comfortable level of fullness, individuals consume more calories from high-fat foods compared to high-carbohydrate

foods (Green, Wales, Lawton, & Blundell, 2000; Stubbs, Harden, et al., 1995; Stubbs, Ritz, Coward, & Prentice, 1995). Passive overconsumption is strongly influenced by the higher energy density of fat relative to carbohydrate and protein (9 vs. ~4 kcal/g, respectively) (Rolls, 2000). Consequently, eating a high-fat energy-dense diet is conducive to overconsumption and a positive energy balance.

Based on the findings from the systematic review in Chapter 2, it can be proposed that habitual physical activity improves the sensitivity of the appetite control system (Beaulieu, Hopkins, Blundell, & Finlayson, 2016). Compared to their inactive counterparts, active individuals decrease their energy intake at an ad libitum test meal following a high-energy preload compared to a low-energy preload (Long et al., 2002; Martins et al., 2013; Martins, Truby, et al., 2007; Van Walleghen et al., 2007). However, preload studies preclude the differentiation between satiation and satiety as separate components of appetite. Additionally, little is known regarding the differences in hedonic mechanisms of appetite control (i.e. food reward and preference for high-fat foods) across different physical activity levels, although research on this topic is emerging (Horner, Finlayson, Byrne, & King, 2016).

4.1.1 Objective & hypotheses

The objective of this study was to assess the satiation response to meals high in fat (HFAT) or carbohydrate (HCHO) in individuals with high levels of physical activity (HiPA) compared to those with low levels of physical activity (LoPA). In addition to measuring the response to passive overconsumption, the effects of physical activity level on several putative determinants of appetite control such as body composition, RMR, daily energy expenditure, fasting appetite-related peptides and eating behaviour traits as secondary outcome measures were examined. It was hypothesized that compared to LoPA, HiPA would: consume less energy in HFAT relative to HCHO, show a greater satiation response (SQ), have a reduced hedonic response to high-fat foods in response to HFAT, and show lower susceptibility to overconsumption on psychological trait measures.

4.2 Methods

4.2.1 Participants

Forty non-obese adults (21 HiPA and 19 LoPA) aged 18-55 years were recruited (39 completed the study; see Table 4-2 for participant characteristics). Groups were matched for age, sex and BMI. Participants were screened for inclusion based on the following criteria: BMI between 20.0-29.9 kg/m^2, non-smoker, weight stable (±2 kg for

previous 3 months), no change in physical activity over the previous 6 months, not currently dieting, no history of eating disorders, not taking any medication known to affect metabolism or appetite, and acceptance of the study foods. In addition, the short-form of the IPAQ (Craig et al., 2003) was used to screen for physical activity levels, with participants only eligible if they engaged in at least 40 minutes of MVPA during 4 days or more per week (HiPA), or less than 40 minutes of MVPA during 1 day per week (LoPA). These criteria were based on a previous study that demonstrated differences in satiety between exercisers and non-exercisers (Long et al., 2002), and have been used in subsequent studies (Horner, Byrne, et al., 2015; Horner et al., 2016). To provide objective evidence of habitual physical activity status, activity was subsequently measured objectively with the SWA. The study was approved by the School of Psychology Ethical Committee at the University of Leeds (15-0181). Participants provided written informed consent prior to taking part and were remunerated £30 on completing the study.

4.2.2 Study design

As shown in Figure 4-1, following a preliminary assessment, HiPA and LoPA participants underwent two laboratory probe days that included a fixed breakfast followed by an ad libitum HFAT or HCHO lunch meal in a randomized crossover design. For the 48 h prior to the three testing sessions, the participants refrained from exercise, and for the 24 h prior, did not consume caffeine or alcohol. On each test day, the participants arrived at the research unit between 07:00-09:00 following a 10-h fast (no food or drink except water). Prior to the first meal day, the participants consumed their habitual diet but were required to record their food intake for 24 h in a diary that was provided to them during the preliminary assessment, and replicated their food intake prior to the subsequent meal day. Compliance with these guidelines were verified upon arrival at the laboratory for each testing session.

During the two meal days, measurements included subjective appetite ratings, hedonic preference (explicit liking and implicit wanting) for high-fat foods, and energy intake at breakfast and at an ad libitum HFAT or HCHO lunch 4 hours later. At the end of the first meal day, the participants were fitted with the SWA, which was worn for 7 days. Each meal day was separated by at least 9 days.

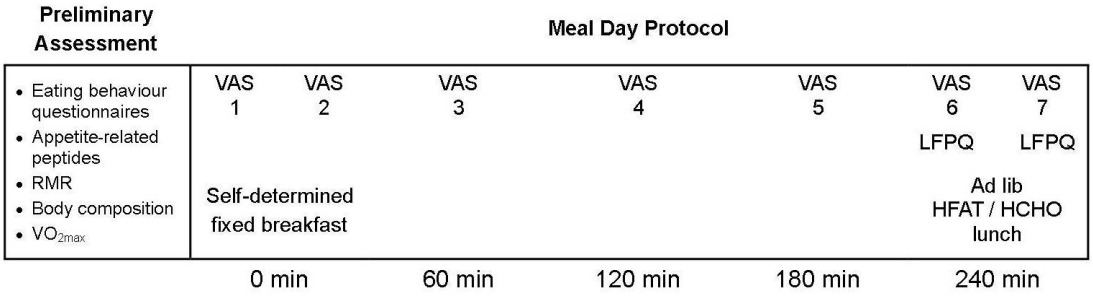

Figure 4-1 Experimental protocol.

4.2.3 Preliminary assessment

Approximately 1 week before the meal days, anthropometrics, body composition (fat mass and fat-free mass), RMR, VO_{2max}, eating behaviour traits (TFEQ, BES and CoEQ) were assessed as previously described in Chapter 3. Additionally, a fasting blood sample was taken for the assessment of leptin, acylated ghrelin, insulin, and glucose.

4.2.3.1 Appetite-related peptides & insulin sensitivity

A fasting blood sample was taken by venepuncture for the assessment of leptin, acylated ghrelin, insulin, and glucose. Blood was drawn in EDTA, serum and fluoride vacutainers. Aprotinin (50 µL/mL blood) was immediately added to the EDTA vacutainer for preservation of ghrelin and centrifuged for 10 minutes at 4ºC at 4000 rpm. The serum tube was left to clot at room temperature for ~60-90 minutes and centrifuged for 10 minutes at 21ºC at 3000 rpm. Plasma and serum obtained were aliquoted and stored at -70ºC until analysis by the Department of Pathology Research & Development at the Leeds Teaching Hospitals NHS Trust, Leeds, UK. All samples were analysed in one batch. Plasma glucose was measured with the ADVIA Chemistry Glucose Oxidase Concentrated assay (Siemens Healthcare Diagnostics Inc., Camberley, UK). Serum insulin was determined with the ADVIA Centaur Insulin assay (Siemens Healthcare Diagnostics Inc., Camberley, UK). Plasma leptin was determined with the Quantikine Human Leptin Immunoassay ELISA kit (R&D Systems Europe Ltd., Abingdon, UK). Acylated ghrelin was measured with the Spi Bio Acylated Ghrelin Express Enzyme Immunoassay kit (Bertin Pharma, Montigny-le-Bretonneux, France). The range of coefficients of variation for intra-assay precision for glucose, insulin, leptin, and acylated ghrelin are 0.2-0.3%, 3.2-4.6%, 3.0-3.3%, and 5.5-10.3%, respectively. Insulin resistance was calculated via the homeostasis model of risk assessment (HOMA) according to the following formula (Matthews et al., 1985):

$$\text{HOMA-IR (\%)} = [\text{Glucose (mmol/L)} * \text{Insulin (mU/L)}]/22.5$$

4.2.4 Meal days

4.2.4.1 Self-determined fixed breakfast

Breakfast during the first meal day was ad libitum with wholegrain cereal, semi-skimmed milk and water served in excess of expected consumption (Figure 4-2). Coffee or tea was also offered (175 g). On the first meal day, the participants were free to self-determine the size of their own breakfasts and were instructed to eat as much or as little as they liked until they reach a comfortable level of fullness. Food items were weighed before and after consumption to the nearest 0.1 g and energy intake was subsequently calculated using energy equivalents for protein, fat and carbohydrate of 4, 9 and 3.75 kcal/g, respectively, from the manufacturers' food labels.

On the second meal day, the quantities consumed by each participant at breakfast on the first meal day were replicated to make the energy content of the meal individually fixed (Figure 4-3), and the participants were instructed to eat the meal in its entirety. The participants were allowed to leave the laboratory in between breakfast and lunch but were not allowed to eat or drink any foods except water from the bottle provided.

Figure 4-2 Ad libitum breakfast (meal day 1)

Figure 4-3 Self-determined fixed breakfast (meal day 2)

4.2.4.2 Ad libitum lunch

Lunch was presented in excess of expected consumption and included HFAT or HCHO rice and yoghurt (Figure 4-4). Water (350 g) was also offered ad libitum. The meals were covertly manipulated to make them HFAT (51% fat) or HCHO (71% carbohydrate; see Table 4-1 for ingredients and macronutrient composition of the meals) but of similar palatability achieved through pilot testing and confirmed by the participants after each meal (see Section 4.3.8). Participants were instructed to eat as little or as much as they wanted until comfortably full. Food items were weighed before and after consumption and energy intake calculated as described in Section 4.2.4.1.

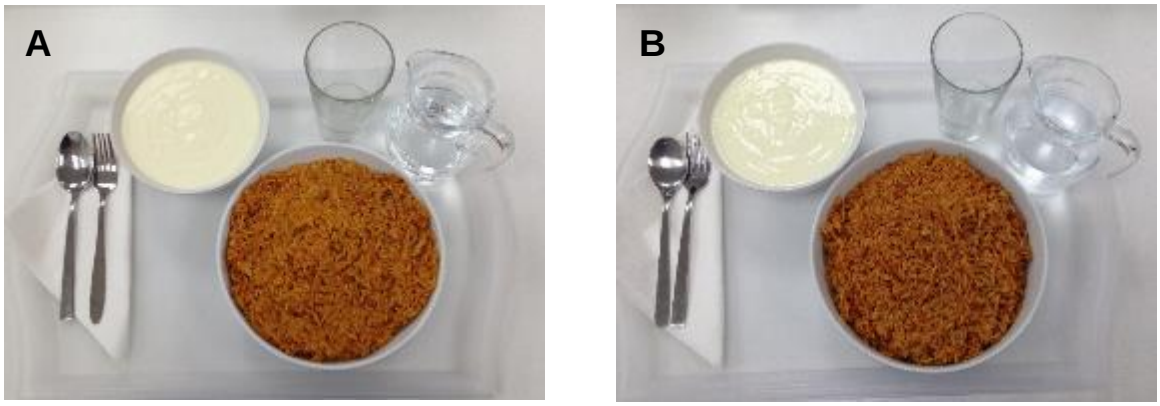

Figure 4-4 High-fat (A) and high-carbohydrate (B) lunch meals.

Table 4-1 Ingredients and macronutrient composition of the HCHO and HFAT rice and yoghurt recipes

	g	kcal	kcal/g	% CHO	% fat	% protein
HCHO	**1701.0**	**2369.4**	**1.39**	**70.5**	**19.8**	**9.7**
Rice recipe	**1116.0**	**1500.7**	**1.34**	**70.2**	**20.0**	**9.8**
Rice	900.0	1418.4	1.58	72.3	18.7	8.9
Vegetable stock	72.0	16.6	0.23	24.4	70.4	5.2
Semi-skim milk	144.0	65.7	0.46	36.4	34.1	29.5
Yoghurt recipe	**585.0**	**868.8**	**1.49**	**70.9**	**19.6**	**9.5**
Natural yoghurt	450.0	362.6	0.81	30.3	46.9	22.8
White sugar	22.5	84.3	3.75	100.0	0.0	0.0
Maltodextrin	112.5	421.9	3.75	100.0	0.0	0.0
HFAT	**1827.1**	**3647.2**	**2.00**	**41.3**	**50.6**	**8.1**
Rice recipe	**1242.0**	**2498.7**	**2.01**	**41.4**	**50.5**	**8.1**
Rice	900.0	1418.4	1.58	72.3	18.7	8.9
Vegetable oil	61.2	550.2	8.99	0.0	100.0	0.0
Water	158.4	0.0	0.00	0.0	0.0	0.0
Double cream	50.4	250.1	4.96	1.3	97.4	1.4
Medium cheddar	72.0	280.1	3.89	1.6	72.7	25.7
Yoghurt recipe	**585.1**	**1148.5**	**1.96**	**41.2**	**50.8**	**8.0**
Low fat yoghurt	375.0	224.3	0.60	44.5	18.1	37.4
Double cream	112.5	558.2	4.96	1.3	97.4	1.4
White sugar	78.8	295.5	3.75	100.0	0.0	0.0
Maltodextrin	18.8	70.4	3.75	100.0	0.0	0.0

4.2.4.3 Passive overconsumption

Passive overconsumption was examined in absolute amounts and also while controlling for differences in TDEE and RMR between LoPA and HiPA. This was expressed 4 ways: 1) absolute difference between HFAT and HCHO meal size in grams (PO_g); 2) absolute difference between HFAT and HCHO meal size in kcal (PO_{kcal}); 3) difference between HFAT and HCHO meal size in kcal accounting for TDEE (PO_{TDEE}); and 4) difference between HFAT and HCHO meal size in kcal accounting for RMR (PO_{RMR}).

4.2.4.4 Appetite ratings

Subjective appetite sensations were assessed before and after each meal and at hourly intervals throughout the meal day via VAS for hunger, fullness, desire to eat and PFC (Flint et al., 2000), as described in Chapter 3. Area under the curve was calculated with the trapezoid rule. The SQ (Green et al., 1997) at the ad libitum meals was calculated for each condition using energy intake at the respective meals, as described in Chapter 3. The post-breakfast SQ (5 time points) was calculated using the mean of the hunger ratings at each time point and energy intake at breakfast of the HCHO and HFAT conditions.

4.2.4.5 Food reward

The LFPQ was administered immediately prior to and after the ad libitum HFAT and HCHO meals to determine scores of implicit wanting and explicit liking for high-fat and low-fat foods as described in Chapter 3. As a measure of hedonic preference for high-fat foods, fat appeal bias was calculated for both liking and wanting by subtracting low-fat scores from high-fat scores. Thus, a positive score indicates greater explicit liking or wanting towards high-fat compared to low-fat foods.

4.2.4.6 Habitual physical activity

Participants were fitted with the SWA during the first meal day whilst in the research unit, as described in Chapter 3. Briefly, the participants were instructed to wear the SWA on their non-dominant arm over 7 days for at least 23 hours per day (awake and asleep, except for the time around showering, bathing or swimming). Compliance was defined as 5 days of wear (including one weekend day) with at least 22 h of verifiable time per day. Proprietary algorithms available in the accompanying software (version 8.0 professional) were used to calculate TDEE, PAL, minutes spent sleeping, sedentary (<1.5 METs) or in light (1.5-2.9 METs), moderate (3.0-5.9 METs) and vigorous (≥ 6.0 METs) physical activity.

4.2.5 Statistical analysis

The sample size was based after the study by Long et al. (2002) who demonstrated in non-obese individuals a difference in food intake between frequent exercisers and non-exercisers. In this preload-test meal design the difference in food intake between groups was ~400kcal with an effect size of d=0.94. A similar effect size in the present study was estimated and it was calculated that n=21 per group would be sufficient to

detect a difference in intake under the high-fat condition with 1-β=0.9 and α=0.05, one-tailed.

A total of 39 participants were included in the final sample (HiPA: 10 males, 10 females; LoPA: 8 males, 11 females), as one male participant in HiPA was excluded due to feeling unwell during the second meal day. Blood samples for 36 participants (20 HiPA and 16 LoPA) were successfully obtained for glucose, insulin and leptin, and because of technical difficulties with the assay, for 22 participants (12 HiPA and 10 LoPA) for ghrelin. SWA data were valid in 36 participants (19 HiPA and 17 LoPA; 92% compliance) due to: no valid weekend days (HiPA female), only 4 valid days (HiPA male) and equipment unavailable (LoPA female).

Independent sample *t*-tests were used to determine differences in participant characteristics and passive overconsumption between LoPA and HiPA groups. Differences in energy intake and SQ were identified with two-way mixed-model ANOVAs, with the between-subject factor of group (HiPA, LoPA) and the within-subject factor of meal condition (HFAT, HCHO). Differences in appetite sensations and food reward (liking and wanting) were identified with three-way mixed-model ANOVAs, with the between-subject factor of group (HiPA, LoPA) and the within-subject factors of meal condition (HFAT, HCHO) and time/food consumption.

4.3 Results

4.3.1 Participant characteristics

Despite there being no group differences in BMI, HiPA had significantly lower body fat and greater fat-free mass and VO_{2max} than LoPA (Table 4-2). The difference in fat mass and RER between HiPA and LoPA approached significance (Table 4-2). There were no significant differences in eating behaviour traits from the CoEQ, BES or TFEQ between HiPA and LoPA (Table 4-3), but differences in restraint approached significance. There were significant differences in IPAQ score between the groups (LoPA: 1332.1 ± 996.2 METs-min•week^{-1} vs. HiPA: 3891.8 ± 1568.8 METs-min•week^{-1}; *p*=.001). As the two groups did not differ in minutes of wear time and sleep, habitual physical activity is presented in minutes per day. The two groups differed significantly in the majority of the measures of habitual physical activity, with HiPA having significantly greater number of daily steps, TDEE, light physical activity, MVPA, PAL, and lower sedentary behaviour than LoPA, as shown in Table 4-4.

Table 4-2 Participant characteristics of LoPA and HiPA groups

	LoPA	**HiPA**	***P*-value**
N	19 (11 F)	20 (10 F)	-
Age (years)	30.4 ± 9.3	29.9 ± 9.6	.85
Height (cm)	166.1 ± 10.8	173.4 ± 10.2	**.04**
BMI ($kg \bullet m^{-2}$)	23.1 ± 2.7	22.6 ± 1.9	.49
Total mass (kg)	64.0 ± 11.9	68.2 ± 11.1	.26
Fat mass (kg)	16.8 ± 6.0	13.1 ± 5.4	.06
Fat-free mass (kg)	47.3 ± 8.6	55.0 ± 11.9	**.03**
Body fat (%)	25.6 ± 7.1	19.7 ± 8.2	**.02**
RMR ($kcal \bullet 24h^{-1}$)	1570.9 ± 296.8	1669.8 ± 226.7	.25
RER	0.75 ± 0.06	0.79 ± 0.07	.06
Waist circumference (cm)	81.2 ± 9.4	79.8 ± 5.5	.59
VO_{2max} ($mL \bullet kg^{-1} \bullet min^{-1}$)	34.7 ± 5.6	50.5 ± 7.5	**.001**
Fasting glucose ($mmol \bullet L^{-1}$)	5.00 ± 0.43[1]	4.84 ± 0.37	.22
Fasting insulin ($mU \bullet L^{-1}$)	8.72 ± 4.48[1]	7.11 ± 3.32	.23
HOMA	2.00 ± 1.25[1]	1.52 ± 0.74	.17
Fasting leptin ($pg \bullet mL^{-1}$)	8561.2 ± 5743.6[1]	8033.4 ± 7712.2	.82
Fasting ghrelin ($pg \bullet mL^{-1}$)	71.8 ± 58.9[2]	47.2 ± 26.4[3]	.25

[1]*n*=16; [2]*n*=10; [3]*n*=12.

Table 4-3 Eating behaviour traits

	LoPA	**HiPA**	***P*-value**
Craving control	59.7 ± 19.6	60.3 ± 23.3	.93
Craving sweet	46.2 ± 23.2	44.5 ± 30.2	.85
Craving savoury	48.9 ± 18.3	45.4 ± 17.0	.54
Positive mood	62.2 ± 11.4	60.4 ± 18.6	.73
Restraint	6.0 ± 3.6	8.8 ± 5.6	.07
Disinhibition	6.2 ± 3.1	6.0 ± 3.8	.89
Susceptibility to hunger	5.7 ± 1.9	6.2 ± 3.0	.57
Binge eating score	8.9 ± 7.3	7.7 ± 6.9	.62

Table 4-4 Habitual physical activity from the SenseWear armband

	LoPA[1]	**HiPA[2]**	***P*-value**
Wear time (min•24h^{-1})	1419.2 ± 8.6	1411.9 ± 17.6	.12
Steps	8236.0 ± 2670.1	11146.9 ± 4258.9	**.02**
TDEE (kcal•24h^{-1})	2368.3 ± 449.8	2967.8 ± 549.0	**.001**
Sleep (min•24h^{-1})	432.1 ± 56.7	415.1 ± 26.6	.27
Light PA (min•24h^{-1})	243.0 ± 91.0	300.5 ± 83.7	.06
Moderate PA (min•24h^{-1})	83.8 ± 27.8	130.6 ± 39.6	**.001**
Vigorous PA (min•24h^{-1})	19.0 ± 14.0	51.6 ± 36.5	**.001**
Total PA (min•24h^{-1})	345.8 ± 112.3	482.8 ± 133.8	**.002**
MVPA (min•24h^{-1})	102.8 ± 37.4	182.2 ± 67.1	**<.001**
Sedentary time (min•24h^{-1})	642.5 ± 100.6	515.0 ± 126.4	**.002**
PAL	1.55 ± 0.13	1.88 ± 0.24	**<.001**

[1]*n*=17; [2]*n*=19. *PA*, physical activity.

4.3.2 Energy intake at breakfast

At breakfast, there were no significant differences in intake between conditions ($F(1,37)=0.08$, $p=.78$) or groups ($F(1,37)=1.47$, $p=.23$) with mean consumption for HiPA being 465.8 ± 208.3 kcal and LoPA being 395.2 ± 147.0 kcal. There were also no differences in beverage consumption between conditions or groups (HFAT LoPA = 271.9 ± 113.1 g, HFAT HiPA = 333.7 ± 127.3 g, HCHO LoPA = 269.6 ± 126.8 g, HCHO HiPA = 294.5 ± 116.2 g; all $p>.05$).

Water intake in between breakfast and lunch was not different between groups, conditions nor was there an interaction (HFAT LoPA = 477.8 ± 291.6 g, HFAT HiPA = 607.8 ± 397.2 g, HCHO LoPA = 578.1 ± 388.5 g, HCHO HiPA = 573.4 ± 356.9 g; all $p>.05$).

4.3.3 Meal size at HFAT and HCHO meals

Meal size at the HFAT and HCHO lunch meals is presented in Figure 4-5. There were no significant main effects of condition ($F(1,37)=1.91$, $p=.18$) or group ($F(1,37)=2.83$, $p=.10$), or interaction between condition and group ($F(1,37)=1.27$, $p=.27$). There were no differences in water intake between conditions, groups nor was there an interaction between the two (HFAT LoPA = 199.6 ± 114.8 g, HFAT HiPA = 216.9 ± 109.8 g, HCHO LoPA = 219.1 ± 114.2 g, HCHO HiPA = 230.7 ± 97.0 g; all $p>.05$).

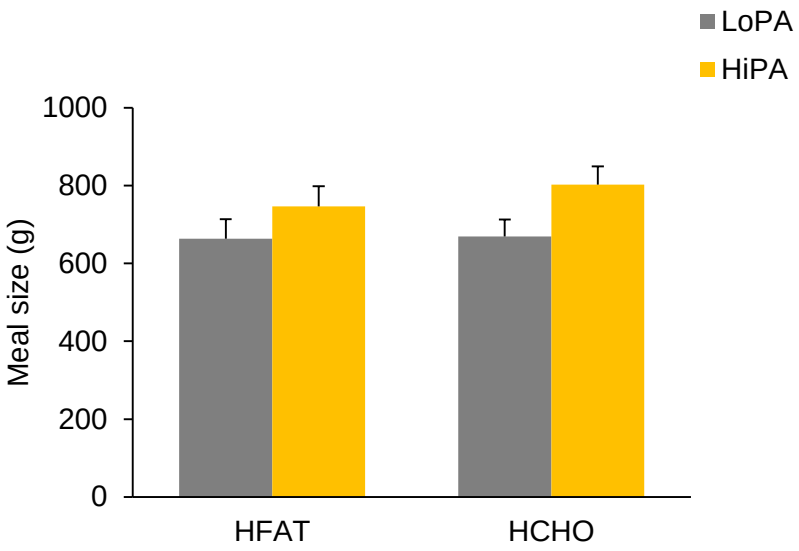

Figure 4-5 Meal size at ad libitum HFAT and HCHO meals.

4.3.4 Energy intake at HFAT and HCHO meals

Energy intake at the lunch meals is presented in Figure 4-6. There was a significant condition effect ($F(1,37)=69.47$, $p<.001$), but no effect of physical activity level ($F(1,37)=2.52$, $p=.12$), or interaction between condition and group ($F(1,37)=0.01$, $p=.92$).

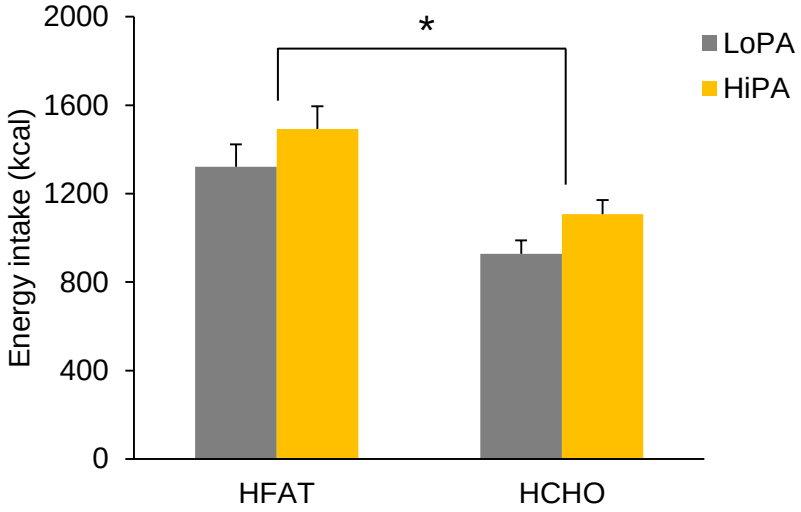

Figure 4-6 Energy intake at ad libitum HFAT and HCHO meals. *Main effect of condition HFAT vs. HCHO $p<.001$.

4.3.5 Passive overconsumption

Data for passive overconsumption are presented in Table 4-5. There were no differences between groups in any of the passive overconsumption parameters.

Table 4-5 Passive overconsumption in LoPA and HiPA

	LoPA	**HiPA**	***P*-value**
PO_g (g)	-5.7 ± 132.7	-55.7 ± 144.0	.27
PO_{kcal} (kcal)	394.1 ± 280.4	385.0 ± 302.1	.92
PO_{TDEE} (%)	16.3 ± 10.0[1]	12.8 ± 9.9	.30
PO_{RMR} (%)	25.5 ± 18.1	22.9 ± 18.2	.66

[1] $n=17$.

4.3.6 Subjective appetite ratings

4.3.6.1 Hunger

Hunger ratings for LoPA and HiPA under the HFAT and HCHO conditions are presented in Figure 4-7a. For baseline hunger, there were no significant effects of condition (F(1,37)=0.50, p=.49) or group (F(1,37)=0.12, p=.73), or interaction between condition and group (F(1,37)=2.72, p=.11).

Throughout the meal day (7 time points), there was a significant effect of time (F(3.25,120.11)=222.65, p<.001), but no significant effect of condition (F(1,37)=3.35, p=.08), group (F(1,37)=0.69, p=.41), condition and group interaction (F(1,37)=0.42, p=.52), time and group interaction (F(3.25,120.11)=0.45, p=.73), condition and time interaction (F(4.10,151.60)=0.33, p=.86), or condition and time and group interaction (F(4.10,151.60)=1.04, p=.39).

For the area under the curve (AUC) ratings of hunger throughout the meal day (Figure 4-8a), there were no significant effects of condition (F(1,37)=1.96, p=.17), group (F(1,37)=0.76, p=.39), or interaction between condition and group (F(1,37)=0.01, p=.93).

4.3.6.2 Fullness

Ratings of fullness for LoPA and HiPA under the 2 conditions are presented in Figure 4-7b. For baseline fullness, there were no significant condition effect (F(1,37)=0.31, p=.58), group effect (F(1,37)=0.09, p=.77), or interaction (F(1,37)=0.23, p=.63).

Throughout the meal day, there was a significant effect of time (F(3.14,116.28)=190.15, p<.001), but no significant effect of condition (F(1,37)=1.09, p=.30), group (F(1,37)=1.20, p=.28), condition and group interaction (F(1,37)=1.86, p=.18), time and group interaction (F(3.14,116.28)=1.25, p=.30), condition and time interaction (F(4.41,163.15)=0.81, p=.57), or condition and time and group interaction (F(4.41,163.15)=1.16, p=.33).

For fullness AUC (Figure 4-8b), there were no significant effect of condition (F(1,37)=1.51, p=.23), group (F(1,37)=1.91, p=.18), or interaction between condition and group (F(1,37)=1.90, p=.18).

4.3.6.3 Desire to eat

Ratings of desire to eat are presented in Figure 4-7c. For baseline ratings, there were no significant effect of condition (F(1,37)=0.14, p=.71) or group (F(1,37)=0.59, p=.45), but there was a significant interaction between condition and group (F(1,37)=4.90,

p=.03), where desire to eat in HCHO relative to HFAT was greater in HiPA and lower in LoPA. Post hoc pairwise comparisons revealed that during HCHO, HiPA had non-significant greater baseline desire to eat compared to HFAT ($F(1,37)= 3.42$, $p=.07$) and LoPA ($F(1,37)=3.33$, $p=.08$).

Throughout the meal day, there was a significant effect of time ($F(3.51,130.03)=179.91$, $p<.001$), and condition and group interaction ($F(1,37)=8.23$, $p=.01$), with HiPA having greater desire to eat during HCHO relative to HFAT ($p=.02$). There were no significant effect of condition ($F(1,37)=0.95$, $p=.34$), group ($F(1,37)=0.93$, $p=.34$), time and group interaction ($F(3.51,130.03)=1.15$, $p=.34$), condition and time interaction ($F(3.74,138.53)=0.43$, $p=.77$), or condition and time and group interaction ($F(3.74,138.53)=1.38$, $p=.35$). When change from baseline scores were calculated to account for differences in baseline ratings, the condition and group interaction did not remain significant ($F(1,37)=2.12$, $p=.15$).

For desire to eat AUC (Figure 4-8c), there were no significant effect of condition ($F(1,37)=0.60$, $p=.44$), group ($F(1,37)=1.17$, $p=.29$), or interaction between condition and group ($F(1,37)=3.85$, $p=.06$).

4.3.6.4 Prospective food consumption

Ratings of PFC are presented in Figure 4-7d. For baseline ratings, there were no significant effect of condition ($F(1,37)=0.03$, $p=.86$), group ($F(1,37)=0.18$, $p=.68$), or interaction between condition and group ($F(1,37)=0.77$, $p=.39$).

Throughout the meal day, there was a significant effect of time ($F(3.51,129.85)=147.80$, $p<.001$), but no significant effect of condition ($F(1,37)=2.19$, $p=.15$), group ($F(1,37)=0.63$, $p=.43$), condition and group interaction ($F(1,37)=3.90$, $p=.06$), time and group interaction ($F(3.51,129.85)=0.90$, $p=.46$), condition and time interaction ($F(3.71,137.20)=0.83$, $p=.50$), or condition and time and group interaction ($F(3.71,137.20)=1.32$, $p=.27$).

For the PFC AUC (Figure 4-8d), there were no significant effect of condition ($F(1,37)=2.30$, $p=.14$), group ($F(1,37)=0.97$, $p=.33$), or interaction between condition and group ($F(1,37)=3.75$, $p=.06$).

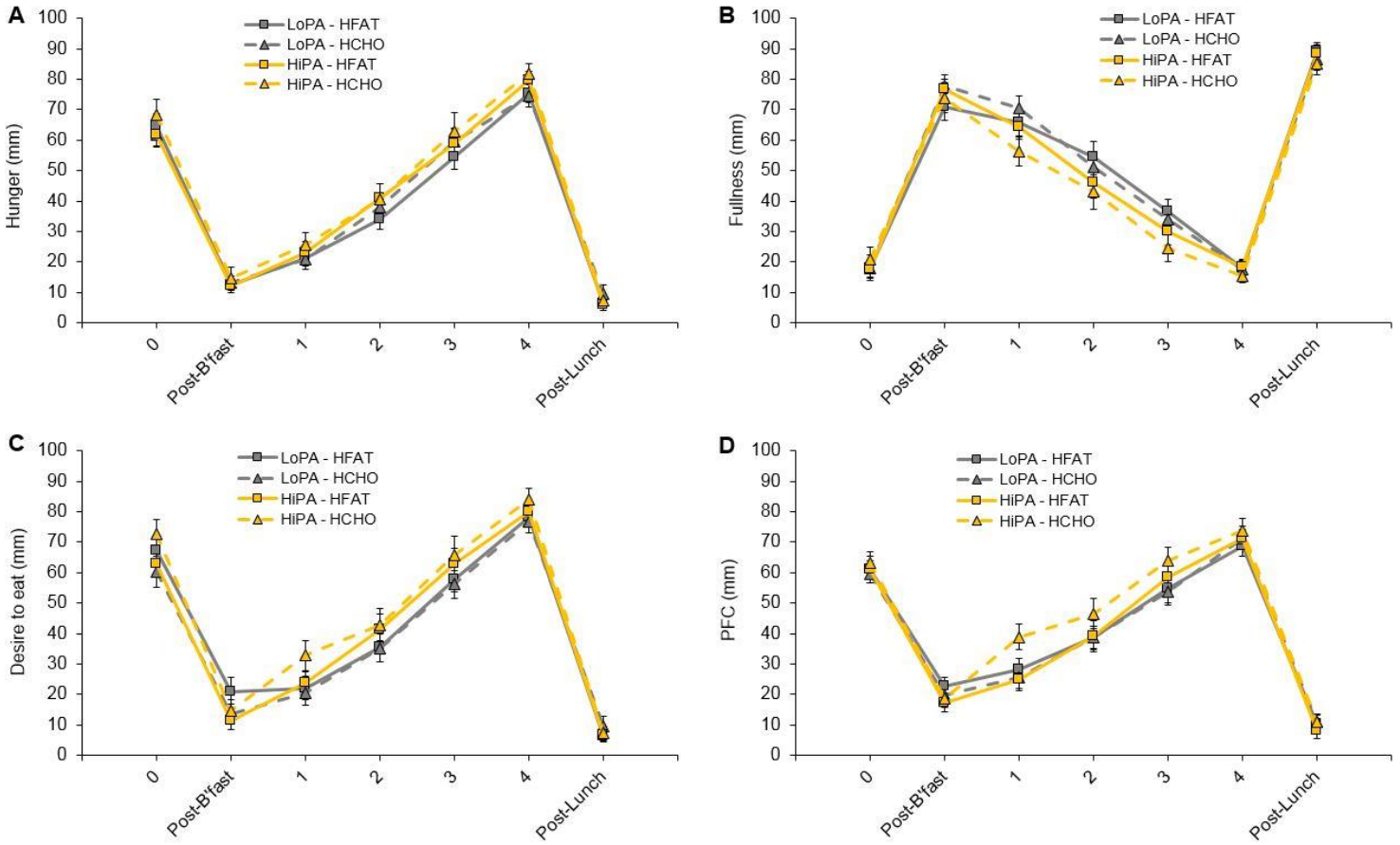

Figure 4-7 Hourly and post-meal **r**atings of hunger (A), fullness (B), desire to eat (C) and prospective food consumption (PFC; D) throughout the HFAT and HCHO meal days.

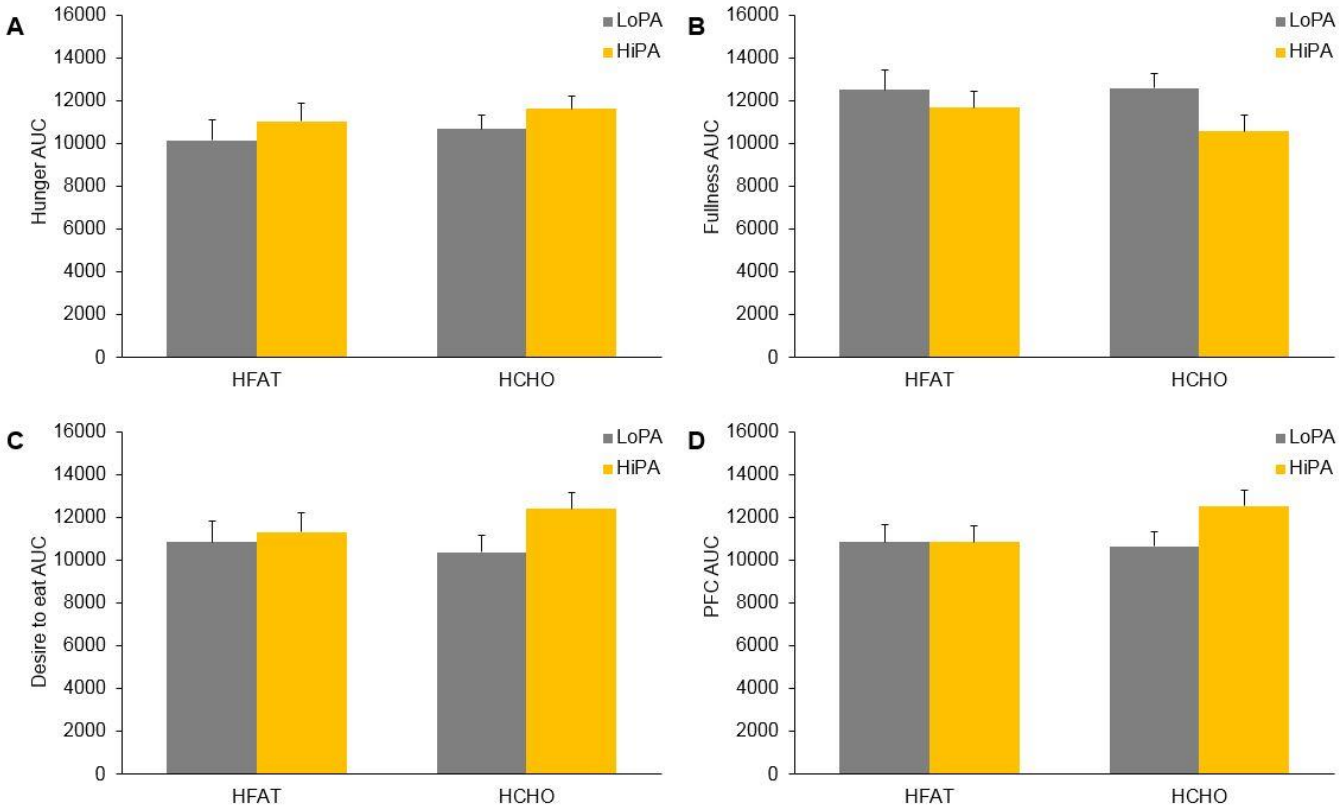

Figure 4-8 Area under the curve (AUC) for ratings hunger (A), fullness (B), desire to eat (C) and prospective food consumption (PFC; D) throughout the HFAT and HCHO meal days.

4.3.7 Satiety quotient

For SQ post-breakfast to pre-lunch (5 time points; Figure 4-9), there was a significant effect of time (F(1.53,56.52)=79.31, p<.001), but no effect of group (F(1,37)=0.68, p=.41) or time and group interaction (F(1.53,56.52)=0.24, p=.73).

For SQ at lunch (Figure 4-10), there was a significant effect of condition (F(1,37)=15.46, p<.001), but no effect of group (F(1,37)=0.62, p=.44) or interaction between condition and group (F(1,37)=0.02, p=.88).

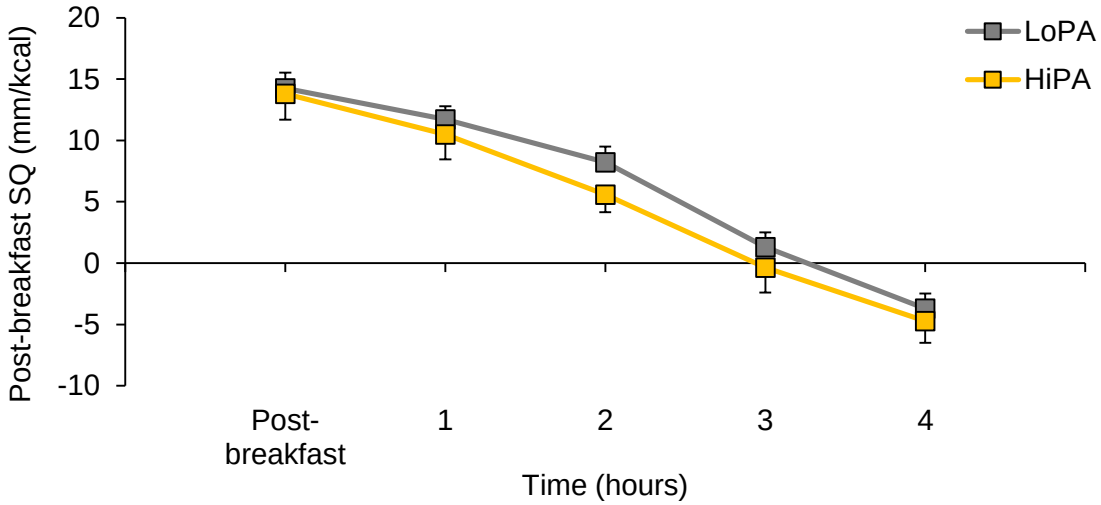

Figure 4-9 Satiety quotient following breakfast as a marker of post-meal satiety.

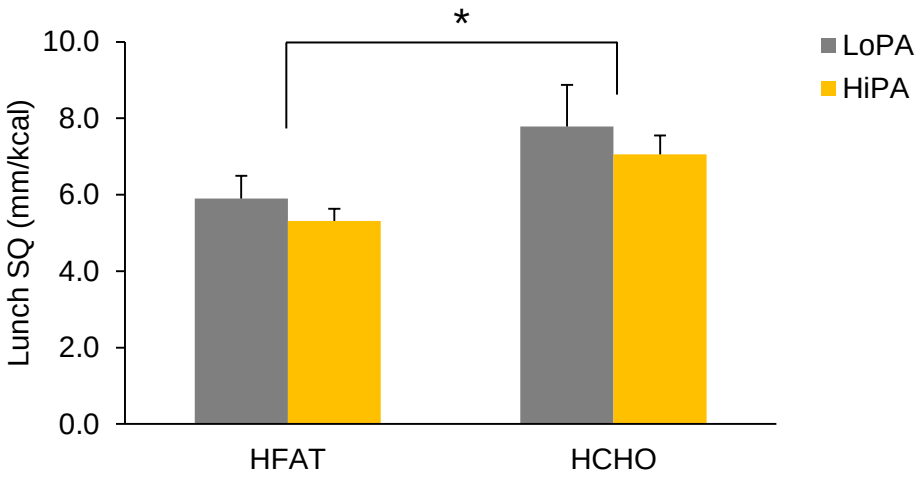

Figure 4-10 Satiety quotient at HFAT and HCHO meal as a marker of within meal satiation. *Main effect of condition HFAT vs. HCHO p<.001.

4.3.8 Palatability ratings

There were no significant effects of condition, group, or interaction between condition and group (p>.05 for all) in palatability ratings for the rice and yoghurt during the HFAT and HCHO meal days (Table 4-6).

Table 4-6 Palatability ratings of the HFAT and HCHO rice and yoghurt

	HFAT		**HCHO**	
	LoPA	**HiPA**	**LoPA**	**HiPA**
Rice				
Savoury	69.8 ± 22.5	71.1 ± 18.5	66.7 ± 22.6	74.2 ± 18.5
Tasty	64.1 ± 23.0	66.8 ± 23.5	62.9 ± 20.8	65.3 ± 17.8
Pleasant	60.1 ± 25.5	66.1 ± 22.5	64.9 ± 19.1	65.0 ± 18.8
Filling	77.3 ± 21.3	83.1 ± 17.5	74.8 ± 21.8	81.8 ± 17.8
Satisfying	64.7 ± 24.6	73.3 ± 21.5	62.6 ± 22.2	71.7 ± 22.3
Yoghurt				
Sweet	72.5 ± 14.2	74.4 ± 16.3	73.1 ± 19.1	77.7 ± 11.6
Tasty	70.1 ± 16.7	71.8 ± 16.1	70.2 ± 19.6	72.3 ± 18.7
Pleasant	67.4 ± 21.3	72.7 ± 15.1	71.2 ± 20.5	73.4 ± 19.5
Filling	49.3 ± 23.7	56.3 ± 25.3	51.0 ± 25.1	60.2 ± 28.1
Satisfying	63.9 ± 20.8	65.2 ± 20.8	65.4 ± 22.7	67.2 ± 25.8

4.3.9 Food reward

Liking and wanting for high-fat relative to low-fat foods pre- and post-lunch did not differ between conditions or groups, nor were there any condition and group interactions (p>.05 for all; Table 4-7).

From pre- to post-lunch, there was a significant main effect of food consumption for liking and wanting (p<.001), such that the preference for high-fat foods relative to low-fat foods decreased from the hungry to the fed state, but there were no main effects of group, condition or interaction effects (p>.05 for all; Table 4-7).

Table 4-7 Liking and wanting pre- and post-lunch, and change from pre- to post-lunch

	HFAT		**HCHO**	
	HiPA	**LoPA**	**HiPA**	**LoPA**
Pre-Lunch				
Liking	3.5 ± 17.1	7.6 ± 16.1	1.6 ± 19.2	5.8 ± 14.5
Wanting	10.2 ± 42.7	21.7 ± 30.5	12.8 ± 40.3	22.2 ± 28.9
Post-Lunch				
Liking	-5.3 ± 13.1	-2.8 ± 16.5	-3.7 ± 14.0	-0.6 ± 13.3
Wanting	-13.2 ± 31.2	-7.1 ± 30.5	-17.5 ± 33.0	-2.4 ± 31.6
Change*				
Liking	-8.8 ± 14.5	-10.4 ± 12.5	-5.2 ± 18.0	-6.4 ± 13.2
Wanting	-23.4 ± 39.3	-28.8 ± 28.1	-30.3 ± 34.9	-24.7 ± 29.3

Note: positive scores indicate greater liking or wanting towards high-fat compared to low-fat foods.

*Main effect of food consumption pre- vs. post-lunch p<.001.

4.4 Discussion

This is the first study to investigate satiation and passive overconsumption in individuals with high and low physical activity levels within a multi-level appetite control framework. The data revealed distinct differences in free-living physical activity and body composition between HiPA and LoPA despite similar BMI. However, for both HiPA and LoPA, the nutritional manipulation of increasing dietary fat (and energy density) led to a similar level of passive overconsumption. In both groups, greater energy intake was seen in HFAT compared to HCHO, without any concurrent changes in appetite sensations or preference for high-fat foods in the hungry and fed state.

4.4.1 Physical activity, body fat and appetite control

It is important to emphasise the contribution of low levels of physical activity to the accumulation of body fat. This study has shown in a non-obese sample that HiPA have greater fat-free mass and lower fat mass compared to LoPA at the same BMI. This supports the role of physical activity for improving body composition and in weight management (Donnelly et al., 2009; Shaw et al., 2006; Stiegler & Cunliffe, 2006). Over time, there exists a dose-response relationship between physical activity level and body weight, such that low levels of physical activity result in greater gains in body weight (i.e. body fat) (Jakicic, Marcus, Lang, & Janney, 2008). An accumulation of body fat leads to insulin resistance and is proposed to be detrimental to satiety signalling (Flint et al., 2007; Speechly & Buffenstein, 2000). In inactive overweight and obese individuals, exercise training reduces fat mass (Caudwell, Gibbons, Hopkins, King, et al., 2013; King et al., 2009) and also alters the release of appetite-related peptides (Martins et al., 2010; Martins et al., 2013), improves insulin and leptin sensitivity (Dyck, 2005; Goodyear & Kahn, 1998; Steinberg et al., 2004), and enhances satiety (measured by the SQ) over several hours after a meal (King et al., 2009). Thus, regular physical activity could sensitize the appetite control system by increasing postprandial sensations of satiety (Blundell, Gibbons, et al., 2015).

This study suggests that, in non-obese individuals, higher levels of habitual physical activity do not mitigate the passive overconsumption response when exposed to a high-fat meal. Interestingly, previous studies conducted in non-obese participants have shown enhanced satiety at higher levels of habitual physical activity without large differences in group characteristics in terms of BMI, eating behaviour traits and insulin sensitivity (Long et al., 2002; Martins, Truby, et al., 2007). Larger disturbances in the putative determinants of appetite control, including body composition, leptin, ghrelin, insulin sensitivity, control over eating, disinhibition, and food reward may be required

to affect satiation and result in overconsumption. These differences in findings emphasise the importance of distinguishing between separate appetite-related processes when examining the impact of physical activity on food intake. Based on these observations, it can be speculated that habitual physical activity may differentially affect the processes of satiation and satiety. While higher levels of habitual physical activity appear to enhance postprandial satiety responsiveness, it is possible that factors other than physical activity (e.g. meal characteristics and cognitive factors) have a stronger influence on satiation. That said, it is plausible that a greater accumulation of body fat and/or lower levels of physical activity than observed in the present study may be necessary to dysregulate satiation and impact on meal size.

4.4.2 Physical activity and passive overconsumption

The passive overconsumption paradigm used in this study achieved several outcomes. Firstly, increasing the fat content (and energy density) of a food led to an increase in energy intake. Secondly, non-obese individuals with similar BMI but differing in levels of physical activity had similar satiation response to meals varying in fat. Thirdly, SQ differed across the HFAT and HCHO conditions, but not between physical activity levels. This demonstrates that per calorie consumed, fat produced a smaller suppression of hunger at the test meal than carbohydrate. These data corroborate previous studies on passive overconsumption via weak satiation and further illustrate the importance of reducing dietary fat (and energy density) to avoid positive energy balance and ultimately weight gain (Blundell & MacDiarmid, 1997; Rolls, 2000). This is not to undermine the contribution of regular physical activity to energy balance, as it is significant as discussed above, but it exemplifies that diet and activity go hand in hand. Indeed, evidence suggests that higher levels of energy expenditure (i.e. habitual physical activity) are beneficial for the regulation of energy balance (Blundell, 2011). A higher energy flux (i.e. higher levels of absolute daily energy expenditure and intake) may also be helpful in mitigating episodes of overconsumption and fluctuations in energy intake (Hill, 2006; Hume, Yokum, & Stice, 2016). For example, Murgatroyd et al. (1999) showed that imposing sedentary behaviour and an ad libitum diet containing 60% energy from fat resulted in a daily positive energy balance of approximately 1000 kcal more than a day with imposed exercise. In the current sample, free-living TDEE as measured by SWA was significantly greater in HiPA than LoPA (600 kcal more per day). Even when accounting for these differences in TDEE with the various indices of passive

overconsumption (Table 4-5), the response to passive overconsumption did not differ. This may have been because energy intake was only measured at one meal.

Previously, Caudwell, Finlayson, et al. (2013) found that after a 12-week exercise-training intervention (5 days per week, 500 kcal per session), overweight and obese individuals significantly lowered energy intake at a high-energy-density test meal (~4 kcal/g, >50% energy from fat) but not at a low-energy-density test meal (~2.4 kcal/g, <25% energy from fat). Thus, adiposity levels may be an important contributor to passive overconsumption as differences in energy intake between lean and obese males have been observed at a test meal following a high-fat high-energy preload compared to a low-fat low-energy preload, where the lean group subsequently compensated for the additional energy from fat whereas the obese group did not (Speechly & Buffenstein, 2000). Furthermore, studies comparing appetite control between active and inactive individuals have measured satiety using preload-test meal paradigms, which led to the proposition in Chapter 2 that physically active individuals have an increased sensitivity to the energy density of foods (Beaulieu et al., 2016). In light of the results of the current study, in non-obese individuals, it is possible that this effect is attributable to mechanisms mediating satiety but not satiation.

In terms of food reward, HiPA and LoPA did not differ in their hedonic preference for high-fat foods (liking and wanting) when hungry or after eating the HFAT and HCHO meals. However, a recent study showed differences in other markers of liking and wanting using the LFPQ between active and inactive males; but the two groups were not matched for BMI and differed much more in body composition than the current study (Horner et al., 2016). The current data showed that HiPA had a tendency for greater restraint score than LoPA, which suggests more cognitive restriction of food intake. Regardless, both groups behaved similarly at the HFAT and HCHO test meals, highlighting the strong environmental influence of dietary fat on energy intake. Independent effects of fat and energy density in passive overconsumption have been observed. It appears that energy density is a stronger driver of passive overconsumption than fat itself because when the energy density of high-fat and high-carbohydrate meals are matched, energy intake is similar (Rolls, 2000; Stubbs, Harbron, & Prentice, 1996). In fact, Hopkins, Finlayson, et al. (2016). have recently shown independent and positive associations between energy expenditure (via RMR) and energy density with daily energy intake.

4.4.3 Limitations

There are a number of limitations to take into account in the present study. Firstly, passive overconsumption was measured using a single meal and limits the

extrapolation of findings beyond that meal. Any compensation in the post-ingestive period remains unknown. As previous studies reported differences in satiety between active and inactive individuals (Long et al., 2002; Martins et al., 2013; Martins, Truby, et al., 2007; Van Walleghen et al., 2007), an effect might have been observed in the hours after consuming the HFAT meal, but this was outside the scope of the present study and needs to be addressed in future studies. Secondly, while objective measurement of physical activity was taken after the participants were included in the study and confirmed distinct physical activity levels between HiPA and LoPA, classification of the groups was based on the IPAQ (self-report) and might have confounded the groups. Other potential confounders not taken into account that may have also affected the results include levels of fat mass, fat-free mass, and dietary restraint. Thirdly, the relatively small number of participants and large inter-individual variability in responses may have resulted in the study being underpowered to detect significant differences. Furthermore, while it was attempted to match the groups by sex, the final sample included a slightly greater proportion of women in the LoPA group compared to the HiPA group (57% vs. 50%, respectively), which may account for the some of the differences in body composition observed. However, when sex was added as a covariate, the significant differences fat-free mass and percentage body fat remained.

4.4.4 Conclusions

This study provides evidence to support the beneficial effects of high levels of habitual MVPA (≥4 days/wk) on body composition, but did not reveal differences in passive overconsumption between non-obese individuals with high and low levels of physical activity matched for BMI. This may help to clarify the differential role of physical activity in the distinct processes of satiation and satiety. While satiety appears to be enhanced with higher levels of physical activity (Beaulieu et al., 2016), it is likely that other factors have a stronger influence on satiation. However, it still remains unknown if the lack of observed effect on satiation in LoPA extends to individuals with a greater accumulation of body fat (obese). Nevertheless, in non-obese individuals, these data suggest that a high-fat meal overpowers any physiologic or behavioural influence of physical activity level on eating behaviour, highlighting the importance of a healthy diet in maintaining adequate appetite control and body weight in an obesogenic food environment.

Chapter summary:

- Despite being matched for BMI, individuals with high and low levels of physical activity differ in body composition.
- Highly active individuals do not have improved satiation or resistance to passive overconsumption of energy compared to less active non-obese individuals with similar BMI.
- Consumption of covertly manipulated HFAT and HCHO foods reduced hedonic preference for fat to a similar degree, regardless of physical activity level.
- A greater accumulation of body fat and/or lower levels of physical activity may be necessary to impact on satiation.

4.5 Measured MVPA sub-analysis

As shown in Figure 4-11, there were a number of participants from the previous study classified by the IPAQ that fell into lower or higher levels of physical activity according to measured MVPA from the SWA. Because of this limitation regarding the classification of the groups based on the IPAQ, a sub-analysis was performed to assess whether groups classified by objectively assessed physical activity would show similar characteristics (i.e. body composition, appetite-related peptides, eating behaviour traits) and respond similarly to the passive overconsumption challenge (i.e. energy intake, passive overconsumption, SQ and food reward) as the original groups based on the IPAQ (self-report).

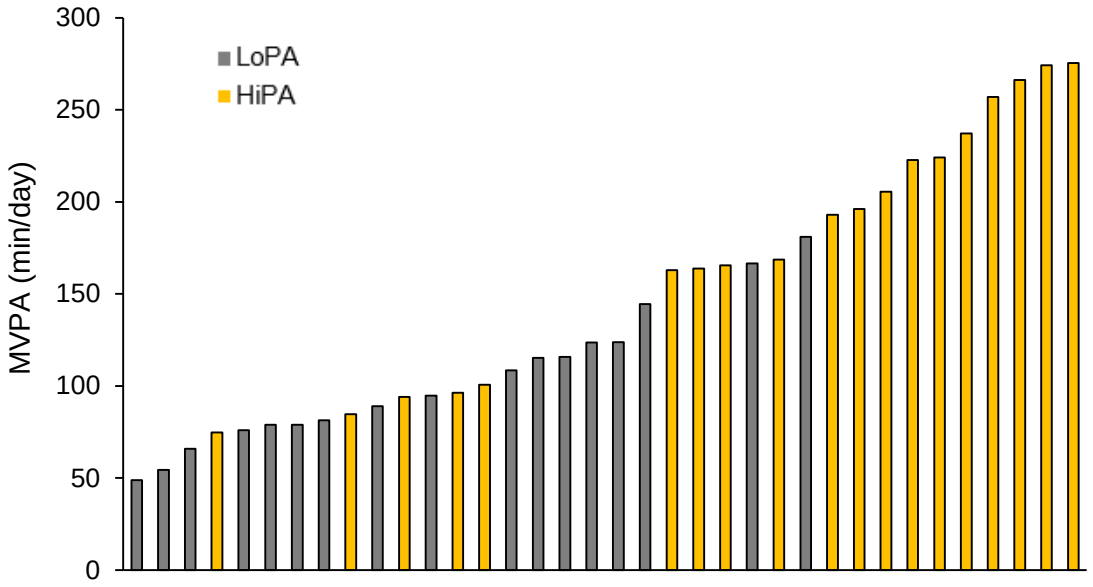

Figure 4-11 Objectively-measured daily minutes of moderate-to-vigorous physical activity by the SWA in individuals classified according to the IPAQ into low (LoPA) and high (HiPA) levels of physical activity.

4.5.1 Results

Thirty-six participants were grouped by sex-specific tertiles of measured daily MVPA obtained from the SWA, and the lower (LoMVPA) and higher (HiMVPA) tertiles were chosen for the current sub-analysis to avoid the overlapping participants in the middle tertile. For males, LoMVPA corresponded to <108 min MVPA/day and HiMVPA to >193 min MVPA/day, while for females, LoMVPA corresponded to <90 min MVPA/day and HiMVPA to >168 min MVPA/day. The redistribution of participants is shown in Table 4-8.

Table 4-8 Redistribution of self-reported IPAQ classification (LoPA and HiPA) into tertiles of objectively-based MVPA from the SWA (LoMVPA, ModMVPA, HiMVPA).

	LoMVPA	**ModMVPA**	**HiMVPA**
LoPA	9	7	1
HiPA	3	5	11

The group characteristics are shown in Table 4-9. The high and low MVPA groups had significant differences in body composition, with HiMVPA having a lower BMI, fat mass and percent body fat than LoMVPA. HiMVPA also had a lower RER and greater VO_{2max} than LoMVPA. The difference in fasting insulin and HOMA between groups approached significance. In terms of eating behaviour traits, there were no significant group differences in scores from the BES, CoEQ or TFEQ (all $p>.05$).

Table 4-9 Group characteristics of lower (LoMVPA) and upper (HiMVPA) tertiles of measured physical activity

	LoMVPA	**HiMVPA**	***P*-value**
n	12 (6 F)	12 (6 F)	
Age (years)	32.2 ± 10.4	27.3 ± 8.7	.22
Height (cm)	173.1 ± 10.8	173.3 ± 8.8	.98
BMI ($kg \bullet m^{-2}$)	24.0 ± 2.3	21.7 ± 1.2	**.008**
Total mass (kg)	72.6 ± 13.5	65.5 ± 9.1	.15
Fat mass (kg)	19.3 ± 5.4	11.2 ± 3.0	**<.001**
Fat-free mass (kg)	53.3 ± 12.8	54.3 ± 10.6	.83
Body fat (%)	26.9 ± 7.4	17.7 ± 5.8	**.003**
RMR ($kcal \bullet 24h^{-1}$)	1570.5 ± 337.0	1710.1 ± 173.9	.22
RER	.81 ± .07	.75 ± .04	**.04**
Waist circumference (cm)	86.0 ± 8.2	77.4 ± 4.6	**.005**
VO_{2max} ($mL \bullet kg^{-1} \bullet min^{-1}$)	36.7 ± 9.4	53.1 ± 7.8	**<.001**
Fasting glucose ($mmol \bullet L^{-1}$)	4.87 ± .31	4.86 ± .47	.97
Fasting insulin ($mU \bullet L^{-1}$)	8.23 ± 3.11	6.06 ± 2.24	.07
HOMA	1.81 ± .81	1.30 ± .48	.08
Fasting leptin ($pg \bullet mL^{-1}$)	9422.8 ± 6197.2[1]	5545.2 ± 5447.5	.13
Fasting ghrelin ($pg \bullet mL^{-1}$)	66.7 ± 36.4[2]	40.8 ± 27.3[3]	.14

[1]*n*=10; [2]*n*=6; [3]*n*=9.

For meal size (Figure 4-12), there were no significant main effect of condition ($F(1,22)=0.05$, $p=.82$) or MVPA group ($F(1,22)=0.40$, $p=.53$), but there was an interaction between condition and MVPA group ($F(1,22)=5.48$, $p=.03$), where HiMVPA consumed a smaller meal size in HFAT whereas the opposite occurred for LoMVPA. Post hoc pairwise comparisons revealed that for LoMVPA, the larger meal size in HFAT relative to HCHO approached significance ($F(1,22)= 3.30$, $p=.08$). The interaction effect persisted when controlling for BMI, fat mass or percentage body fat.

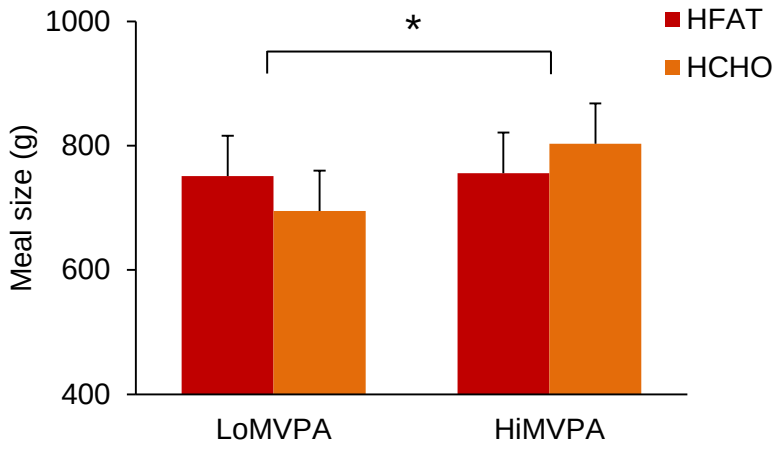

Figure 4-12 Meal size at HFAT and HCHO ad libitum meals LoMVPA and HiMVPA groups. *Significant interaction between condition and MVPA group $p<.05$.

For energy intake (Table 4-10), there were a significant main effect of condition ($F(1,22)=90.13$, $p<.001$), but no effect of MVPA group ($F(1,22)=0.30$, $p=.59$) or interaction between condition and MVPA group ($F(1,22)=2.09$, $p=.16$).

Table 4-10 Energy intake at HFAT and HCHO ad libitum meals in groups of LoMVPA and HiMVPA.

	LoMVPA	**HiMVPA**
HFAT (kcal)*	1499.4 ± 477.7	1510.9 ± 426.6
HCHO (kcal)	959.1 ± 321.4	1113.3 ± 299.8

*Main effect of condition HFAT vs. HCHO $p<.001$.

For passive overconsumption, there were significant differences between MVPA groups for PO_g and PO_{TDEE}, while differences approached significance for PO_{RMR} with HiMVPA having lower passive overconsumption scores than LoMVPA, as shown in Table 4-11.

Table 4-11 Passive overconsumption between high and low tertiles of MVPA

	LoMVPA	**HiMVPA**	***P*-value**
PO (grams)	57.0 ± 64.6	-46.8 ± 139.3	**.03**
PO (kcal)	540.3 ± 194.3	397.7 ±281.8	.16
PO_{TDEE} (%)	21.9 ± 6.3	12.8 ± 8.9	**.009**
PO_{RMR} (%)	34.9 ±11.9	23.4 ± 17.0	.07

For SQ at the HCHO and HFAT meals, there was also a significant effect of condition ($F(1,22)=11.64$, $p=.003$), but no effect of MVPA group ($F(1,22)=0.13$, $p=.72$), or condition and MVPA group interaction ($F(1,22)=0.15$, $p=.71$). For liking, there was a significant effect of food consumption, with a decrease in liking for high-fat foods after lunch ($F(1,22)=10.34$, $p=.004$), and a main effect of group ($F(1,22)=5.28$, $p=.03$), where LoMVPA had significantly lower liking for high-fat foods than HiMVPA (LoMVPA: -5.25 ± 7.67 vs. HiMVPA: 1.94 ± 7.67). There were no other main effects or interactions (all $p>.05$). For wanting, there was a significant effect of food consumption, with a decrease in wanting for high-fat foods after lunch ($F(1,22)=29.43$, $p<.001$), but no other main effects or interactions (all $p>.05$).

4.5.2 Discussion

This sub-sample analysis compared groups based on objective and quantified physical activity. This resulted in the low and high MVPA tertiles showing larger differences in body composition (BMI, fat mass, percentage body fat, and waist circumference), insulin, and insulin sensitivity. While it was speculated in the aforementioned discussion that habitual physical activity may differentially affect the processes of satiation and satiety, this sub-sample analysis provides evidence for the possibility that a greater accumulation of body fat or greater disturbances in other putative determinants of appetite control (such as insulin sensitivity) may be necessary to dysregulate satiation and impact on meal size. Indeed, the data revealed a different response in meal size between LoMVPA and HiMVPA, with LoMVPA consuming a larger meal size (in grams) in HFAT relative to HCHO, whereas the opposite occurred

in HiMVPA. This suggests that satiation may be weakened at lower levels of physical activity depending upon a greater accumulation of body fat. Despite this response in meal size, both groups showed a passive overconsumption of energy, but when differences in TDEE and RMR were taken into consideration, passive overconsumption was mitigated in HiMVPA. These larger differences observed in BMI, body fat, waist circumference and insulin sensitivity between groups may have mediated this effect on satiation, but this is only an interpretation and needs to be addressed more intensively in future studies. Moving forward, groups based on objective assessment of MVPA should be created to eliminate the potential lack of accuracy of self-reported physical activity level.

Sub-sample analysis summary:

- The lower and upper tertiles of objectively measured physical activity differed more in terms of BMI, fat mass, waist circumference and insulin sensitivity.
- The low active group showed a blunted satiation response compared to more active individuals, with a greater meal size (in grams) at HFAT relative to HCHO.
- This analysis suggests that the dysregulation of satiation in individuals with low levels of physical activity could be dependent upon a greater accumulation of body fat or related disturbances in other putative determinants of appetite control such as insulin sensitivity.
- Grouping participants based on objective and measured physical activity may provide better insight into the effects of physical activity level on appetite control.

Chapter 5 – Acute effect of objectively-measured physical activity level on satiety, 24-h energy intake and food reward (SCOPE – Short-term Compensation Of Preload Energy)

Chapter aims:

- Investigate the influence of objectively-measured physical activity level on satiety, energy compensation, appetite and food reward following consumption of preloads varying in energy content.
- Examine 24-h energy intake and energy balance in individuals differing in measured habitual physical activity level.

5.1 Introduction

Chapter 4 showed that satiation, measured with a passive overconsumption paradigm comparing energy intake at high-fat and high-carbohydrate meals, may not be influenced by physical activity level in non-obese individuals matched for BMI (K. Beaulieu, M. Hopkins, J. E. Blundell, & G. Finlayson, 2017a). Satiety, however, has been shown to be improved in physically active individuals, again demonstrating the importance of distinguishing between distinct appetite processes such as satiation and satiety. Using a preload-test meal paradigm, studies have found that physically active individuals show better energy compensation than inactive individuals such that they reduce energy intake to offset the difference in energy consumed in the preload (Long et al., 2002; Martins et al., 2013; Martins, Truby, et al., 2007; Van Walleghen et al., 2007). Moreover, measuring the SQ in the hours following a fixed meal, studies have showed that satiety increases after 12 weeks of exercise-training in previously inactive overweight and obese individuals (Caudwell, Gibbons, Hopkins, King, et al., 2013; King et al., 2009). These improvements in satiety signalling may relate to exercise-induced changes in postprandial satiety peptides such as leptin (Guelfi et al., 2013; Martins et al., 2013), insulin (Guelfi et al., 2013; Martins et al., 2010), GLP-1 and PYY (Martins et al., 2010).

However, the beneficial effects of physical activity on satiety were based mainly on food diaries and all on self-reported habitual physical activity (Long et al., 2002; Van Walleghen et al., 2007). Test meals for the assessment of energy intake

under controlled laboratory conditions are preferred over food diaries as the latter are subject to bias and misreporting (Dhurandhar et al., 2014). Additionally, with wearable technologies being more available, objective assessment of habitual physical activity via accelerometry can now readily be used; reducing bias from participants overestimating their physical activity habits (Dhurandhar et al., 2014; Sallis & Saelens, 2000). Furthermore, the preloads used in previous studies were liquid-based and not matched for macronutrient composition, which may affect individuals' compensatory response (Almiron-Roig, Chen, & Drewnowski, 2003; Mattes, 2006).

In addition to an action on homeostatic mechanisms, other mechanisms in which habitual physical activity may affect satiety is the rewarding value of foods (liking and wanting) and hedonic preference for high-fat foods (Horner et al., 2016). These can override physiological satiety signals and lead to overconsumption (Erlanson-Albertsson, 2005).

5.1.1 Objective

The objective of this study was to compare the satiety, 24-h energy intake and food reward response to high-energy (HEP) and low-energy (LEP) preloads relative to a no-energy control preload (NEP) in individuals differing in objectively-measured physical activity. It was hypothesised that more active individuals would have a greater reduction of energy after the HEP relative to LEP compared to their less active counterparts.

5.2 Methods

5.2.1 Participants

Forty-two adults aged 18-55 years were initially recruited for the study, 36 completed the study but due to non-valid SWA data (<22h wear time <5 days), 34 participants were included in the final sample. Participants were screened for inclusion based on the following criteria: BMI between 20.0-29.9 kg/m^2, non-smoker, weight stable (±2 kg for previous 3 months), no change in physical activity over the previous 6 months, not currently dieting, no history of eating disorders, not taking any medication known to affect metabolism or appetite and acceptance of the study foods. In order to recruit three groups of participants that differed in physical activity level (i.e. low: ≤1 day/week, moderate: 2-3 days/week or high: ≥4 days/week), the short-form of the IPAQ (Craig et al., 2003) was used as part of the screening process to estimate

habitual MVPA. Age, sex and BMI were also monitored throughout screening to ensure the groups were similar in these characteristics. Following initial screening, habitual MVPA was then measured and confirmed using the SWA and used to group participants into a posteriori sex-specific tertiles of daily MVPA (low: LoMVPA, moderate: ModMVPA, or high: HiMVPA). Approximately half of the participants remained in their original self-report physical activity group estimated by the IPAQ (45%, 45% and 58%, in the LoMVPA, ModMVPA and HiMVPA tertiles, respectively). For males, LoMVPA corresponded to <112 min MVPA/day and HiMVPA to >148 min MVPA/day, while for females, LoMVPA corresponded to <90 min MVPA/day and HiMVPA to >143 min MVPA/day. This study was approved by the School of Psychology Ethical Committee (15-0382). Participants provided written informed consent prior to taking part and were remunerated £30 upon completing the study.

5.2.2 Study design

Following a preliminary assessment, participants underwent three laboratory probe days (Figure 5-1), in a Latin square design, that included a fixed breakfast followed by a HEP, LEP or NEP, and ad libitum lunch, dinner and snack box meals to examine the 24-h energy intake response to preloads varying in energy content. NEP was used as a baseline condition to assess the response to the HEP and LEP relative to NEP.

For the 24 h prior to the testing sessions, the participants refrained from exercise, and did not consume caffeine or alcohol. On each test day, the participants arrived at the research unit between 07:00-09:00 following a 10-h fast (no food or drink except water). Prior to the first meal day, the participants consumed their habitual diet but were required to record their food intake for 24 h in a diary that was provided to them during the preliminary assessment, and replicated their food intake prior to the subsequent meal days. Compliance with these guidelines were verified upon arrival at the laboratory for each testing session.

During the meal days, subjective appetite ratings were measured before and after each meal and at hourly intervals throughout the day, while food reward was measured with the LFPQ before and after preload consumption. Energy intake at individual meals was measured, and subsequently used to calculate 24-h energy intake. Upon arrival at the laboratory, participants were also fitted with the SWA and wore the monitor until the following morning (~24h) to determine energy expenditure during the meal days. After a fixed energy breakfast, participants returned 3 h later for the consumption of the preloads, 1 h after which they consumed an ad libitum lunch. Dinner was consumed 4 h after lunch and participants were given an ad libitum snack

box for the remainder of the evening. Each meal day was separated by at least seven days.

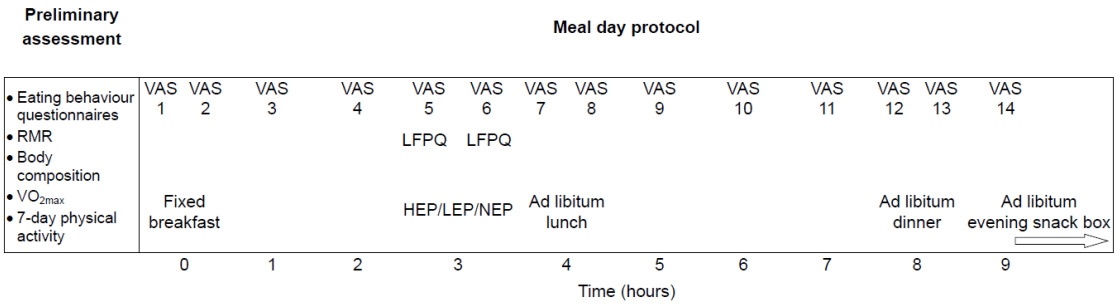

Figure 5-1 Experimental protocol.

5.2.3 Preliminary assessment

At least 8 days before the meal days, RMR, body composition (fat mass, fat-free mass), VO_{2max}, and eating behaviour traits (TFEQ, BES and CoEQ) were assessed as previously described in Chapter 3.

5.2.3.1 Habitual physical activity

Upon completion of the preliminary assessment, participants were fitted with a SWA, as described in Chapter 3. Briefly, the SWA estimates TDEE, PAL, minutes spent sleeping, sedentary, or in light physical activity or MVPA. The SWA was worn for 7 days (day 1 beginning the following day) and removed on the morning of the 8th day.

5.2.4 Meal days

5.2.4.1 Fixed breakfast

During the meal days, participants consumed a standardised, fixed-energy breakfast composed of muesli, natural yoghurt, raisins, currants and honey, calculated to provide 25% of an individual's measured RMR (mean energy content: 398.7 kcal, range 317.1-539.1 kcal; Figure 5-2). The muesli had an energy density of 1.34 kcal/g, with a macronutrient composition of 63.1 % energy from carbohydrate, 21.9 % from fat and 15.0 % from protein. Participants had 15 minutes to consume the meal in its entirety, and food items were weighed before and after consumption to the nearest 0.1g to ensure compliance. Participants were offered one cup (300 g) of either tea, coffee (with or without milk) or water. If they chose to include milk in their tea or coffee (40 g) this was excluded from their breakfast muesli. The beverage they chose on their

first meal day was repeated on the subsequent probe day. Food items were weighed before and after consumption to the nearest 0.1 g and energy intake was subsequently calculated using energy equivalents for protein, fat and carbohydrate of 4, 9 and 3.75 kcal/g, respectively, from the manufacturers' food labels. Upon full consumption of breakfast, participants were instructed not to eat or drink any food until their next meal session except from the bottle of water provided. They were told to refill this bottle when completely empty and tally the number of times they do so. Participants were instructed to return the bottle with any remaining water at the following meal. Participants were allowed to leave the research unit after breakfast and instructed the time at which to return for their morning snack.

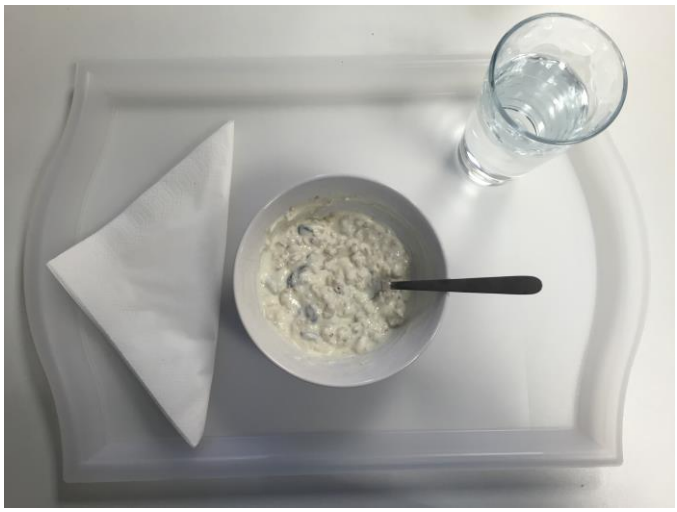

Figure 5-2 Fixed-energy breakfast

5.2.4.2 Preloads

Three hours after breakfast, participants returned to the laboratory and consumed either a porridge HEP (700.5 kcal) or LEP (257.5 kcal) with 150 g of water, or water NEP (445.5 g; Figure 5-3). The porridge preloads differed in energy content, but were of similar macronutrient composition (Table 5-1), weight, volume and palatability. Pilot testing with different participants prior to data collection (n=9) showed no difference in sweetness (HEP: 6.8 ± 1.3 vs. LEP: 6.3 ± 1.4 out of 10; p=.48), liking (HEP: 5.9 ± 2.0 vs. LEP: 6.6 ± 0.7 out of 10; p=.36), pleasantness (HEP: 6.6 ± 1.9 vs. LEP: 6.8 ± 0.4 out of 10; p=.71), and desire to eat (HEP: 4.1 ± 3.2 vs. LEP: 3.6 ± 2.8 out of 10; p=.41) between the two porridge preloads. All preloads were consumed in their entirety within 15 minutes, and were weighed before and after consumption to ensure compliance.

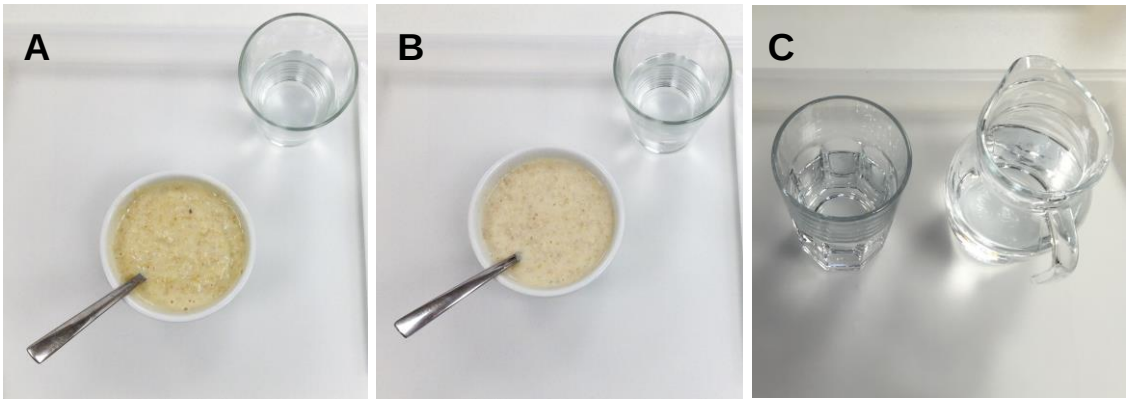

Figure 5-3 High-energy (A), low-energy (B), and no-energy control (C) preloads

Table 5-1 Ingredients and macronutrient composition of the two porridge preloads

	g	kcal	kcal/g	%CHO	%FAT	%PRO
HEP	**295.5**	**700.5**	**2.37**	**39.5**	**46.8**	**13.7**
Porridge oats	30.0	102.3	3.41	66.0	21.1	12.9
Ground almonds	25.0	157.1	6.29	3.9	79.9	16.2
Whey protein	10.0	41.4	4.14	4.5	16.3	79.2
Maltodextrin	45.0	168.8	3.75	100.0	0.0	0.0
Sweetener	0.5	1.8	3.58	98.4	0.0	1.6
Whole milk	160.0	105.1	0.66	27.7	50.9	21.4
Double cream	25.0	124.0	4.96	1.3	97.4	1.4
LEP	**295.5**	**257.5**	**0.87**	**39.1**	**46.4**	**14.5**
Porridge oats	30.0	102.3	3.41	66.0	21.1	12.9
Ground almonds	11.0	69.1	6.29	3.9	79.9	16.2
Maltodextrin	3.0	11.3	3.75	100.0	0.0	0.0
Sweetener	1.3	4.7	3.58	98.4	0.0	1.6
Skimmed milk	50.0	17.4	0.35	54.6	2.7	42.8
Single cream	15.0	29.0	1.93	4.3	88.5	7.2
Greek style yogurt	20.0	23.8	1.19	16.7	69.5	13.8
Water	165.2	0.0	0.00	0.0	0.0	0.0

5.2.4.3 Ad libitum lunch

One hour after the start of the preload, participants consumed an ad libitum lunch, which consisted of a single course tomato and herb risotto mixed with olive oil (1.99 kcal/g, 53.3% carbohydrate, 39.9% fat, 6.8% protein) with a side of chopped cucumber and tomatoes, served in excess of expected consumption (Figure 5-4). The participants were instructed to eat as much or as little as they liked until they reach a comfortable level of fullness. Ad libitum water was also offered (300 g). Food items were weighed before and after consumption to the nearest 0.1 g to determine quantities consumed, and energy intake calculated as described above.

Figure 5-4 Ad libitum lunch meal

5.2.4.4 Ad libitum dinner

Four hours after lunch, participants consumed an ad libitum dinner, consisting of vegetarian chilli mixed with rice, olive oil, and grated cheddar cheese (1.30 kcal/g, 49.8% carbohydrate, 37.4% fat, 12.8% protein) with a side of pineapple pieces, served in excess of expected consumption (Figure 5-5). Ad libitum water was also offered (300 g). Again, participants were instructed that they could eat as much or as little as they liked until they reach a comfortable level of fullness. Food items were weighed before and after consumption to the nearest 0.1 g to determine quantities consumed, and energy intake calculated as previously described.

Figure 5-5 Ad libitum dinner meal

5.2.4.5 Ad libitum snack box

Upon consumption of the dinner, participants were given a snack box containing a selection of pre-weighed foods (strawberry yoghurt, apples, tangerines, cheese crackers, almonds, popcorn, and granola bars; Figure 5-6). Participants were instructed to eat only from this snack box until they went to bed that evening and to return all elements of the snack box, including empty packaging or partially-eaten foods, the following morning.

Figure 5-6 Ad libitum snack box food items

5.2.4.6 Compensation index

The compensation index (COMPX; Johnson & Birch, 1994) was calculated based on the difference in energy content of the HEP and LEP (~440 kcal), and energy intake during the ad libitum meals. This index quantifies the adjustment in energy intake at a test meal following preloads differing in energy content. If an individual adjusts energy intake perfectly to compensate for the preloads, COMPX would be 100%. In contrast, individuals less sensitive to the satiety effects of the nutritional manipulation of the preload would have a COMPX score deviating negatively from 100% (Figure 5-7). COMPX was calculated using the formula below:

$$\text{COMPX (\%)} = \frac{\text{Difference in test meal energy intake}}{\text{Difference in preload energy}} \times 100$$

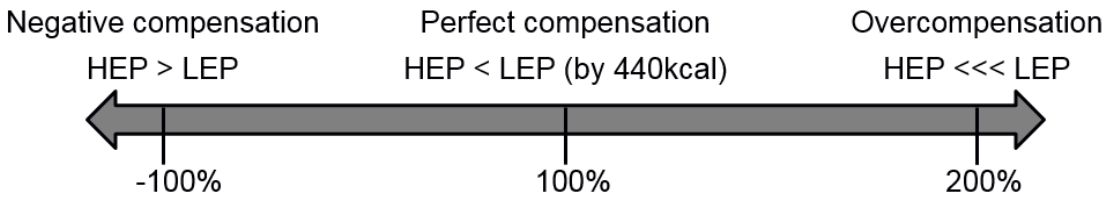

Figure 5-7 Compensation index scale

5.2.4.7 Appetite ratings and satiety quotient

Appetite ratings were assessed before and after each meal, and at hourly intervals throughout the meal day via VAS for hunger, fullness, desire to eat and PFC using the Electronic Appetite Rating System (Gibbons et al., 2011) as described in Chapter 3. To specifically examine the effect of the preloads on satiety, AUC was calculated using the trapezoid rule for the 1-h period following preload consumption (post-preload, 3 time points) and the 2-h period following lunch consumption (post-preload and lunch, 4 time points). The SQ (Green et al., 1997) following consumption of fixed breakfast was calculated as described in Chapter 3 with the mean hunger ratings and energy intake at breakfast from the three conditions.

5.2.4.8 Food reward

The LFPQ was administered pre- and post-preload consumption to determine scores of implicit wanting and explicit liking fat appeal bias to determine preference for high-fat relative to low-fat foods (Finlayson et al., 2008), as described in Chapter 3.

5.2.5 Statistical analysis

The sample size was based after the study by Long et al. (2002) who demonstrated that non-obese high active individuals consumed less after a HEP relative to a LEP (*d*=0.88). A similar effect size in the present study was estimated and it was calculated that *n*=10 per group would be sufficient to detect a difference in intake between HEP and LEP within groups with 1-β=0.8 and α=0.05, one-tailed. Thirty-four participants with compliant SWA data (>22 h of verifiable time per day for at least 5 days, including 1 weekend day) were included in the final sample.

Differences in group characteristics; energy intake, baseline appetite ratings and AUC in the NEP condition, and COMPX between MVPA groups (LoMVPA, ModMVPA, HiMVPA) were determined via one-way ANOVAs. To examine the effect of the preloads, energy intake, appetite sensations and food reward in HEP and LEP relative to NEP were computed. Differences in relative energy intake and appetite AUC were determined via two-way mixed model ANOVA with condition (HEP, LEP) as the within-subject factor and MVPA group as the between-subject factor. Changes in relative food reward were assessed with three-way mixed-model ANOVAs with condition and time (pre- and post-preload consumption) as the within-subject factors and MVPA group as the between-subject factor. Bonferroni post hoc analyses adjusted for multiple comparisons were used when significance was achieved.

5.3 Results

5.3.1 Participant characteristics

The characteristics of the three MVPA groups are presented in Table 5-2. The groups did not significantly differ in age, BMI, body composition, RMR, RER, waist circumference or eating behaviour traits (all $p>.05$), but by design, differed in terms of VO_{2max}, habitual physical activity and sedentary behaviour (Table 5-2 and Table 5-3). Because SWA wear time differed significantly between groups ($p=.03$), ANCOVAs controlling for SWA wear time were conducted for the SWA parameters in Table 5-3.

Table 5-2 MVPA group characteristics

	LoMVPA	**ModMVPA**	**HiMVPA**
n	11 (8 F)	11 (8 F)	12 (8 F)
Age (years)	29.6 ± 10.7	26.0 ± 3.3	28.7 ± 10.0
Height (cm)	165.6 ± 7.1	168.8 ± 8.7	169.8 ± 8.5
BMI ($kg \bullet m^{-2}$)	23.1 ± 2.9	22.7 ± 2.2	22.4 ± 2.1
Total mass (kg)	63.8 ± 11.6	64.8 ± 9.3	64.7 ± 9.3
Fat mass (kg)	17.5 ± 4.5	15.5 ± 5.1	14.6 ± 5.3
Fat-free mass (kg)	46.4 ± 10.3	49.3 ± 11.3	50.1 ± 10.6
Body fat (%)	27.6 ± 6.5	24.5 ± 8.8	22.9 ± 8.0
RMR ($kcal \bullet 24h^{-1}$)	1514.7 ± 225.3	1674.2 ± 274.1	1689.4 ± 313.6
RER	0.75 ± 0.08	0.76 ± 0.08	0.77 ± 0.06
WC (cm)	79.8 ± 9.8	77.4 ± 7.9	77.5 ± 4.9
VO_{2max} ($mL \bullet kg^{-1} \bullet min^{-1}$)	37.0 ± 7.0[a]	43.5 ± 6.8[a,b]	46.4 ± 6.4[b,1]
Binge eating score	10.6 ± 5.8	7.6 ± 6.0	7.8 ± 5.7
Restraint	8.8 ± 5.3	8.1 ± 4.1	8.1 ± 3.3
Disinhibition	6.2 ± 2.6	5.5 ± 3.0	5.3 ± 3.1
Susceptibility to hunger	4.8 ± 3.0	5.3 ± 3.1	4.8 ± 2.6
Craving control	62.2 ± 14.8	65.5 ± 21.9	57.2 ± 19.4
Craving sweet	39.7 ± 18.3	47.1 ± 24.9	47.9 ± 25.9
Craving savoury	48.7 ± 21.0	43.9 ± 23.2	45.0 ± 21.4

Unalike letters indicate difference $p<.01$. [1]n =11.

Table 5-3 Habitual physical activity from the SenseWear Armband

	LoMVPA	ModMVPA	HiMVPA
Wear time (min•24h^{-1})	1415.8 ± 13.5^{a,b}	1420.6 ± 8.4^{a}	1406.7 ± 13.8^{b}
Steps	7828.1 ± 1443.6^{a}	10356.6 ± 2138.9^{b}	12834.9 ± 2271.0^{c}
TDEE (kcal•24h^{-1})	2184.8 ± 394.7^{a}	2435.4 ± 405.3^{a,b}	2706.4 ± 548.8^{b}
Sleep (min•24h^{-1})	435.8 ± 25.1	430.9 ± 17.7	399.2 ± 59.6
Light PA (min•24h^{-1})	214.7 ± 73.3^{a}	253.9 ± 67.6^{a,b}	280.0 ± 73.9^{b}
Moderate PA (min•24h^{-1})	70.0 ± 13.9^{a}	98.3 ± 17.8^{b}	143.1 ± 30.1^{c}
Vigorous PA (min•24h^{-1})	12.7 ± 9.6^{a}	22.3 ± 11.7^{a,b}	30.9 ± 20.5^{b}
MVPA (min•24h^{-1})	82.7 ± 16.2^{a}	120.7 ± 14.8^{b}	174.0 ± 38.6^{c}
Total PA (min•24h^{-1})	297.4 ± 84.9^{a}	374.6 ± 67.9^{a}	454.0 ± 89.9^{b}
SED (min•24h^{-1})	682.3 ± 81.5^{a}	615.1 ± 74.7^{a,b}	553.7 ± 94.0^{b}
PAL	1.49 ± 0.07^{a}	1.62 ± 0.06^{b}	1.78 ± 0.14^{c}

Unalike letters indicate difference $p<.05$. *SED*, sedentary time

5.3.2 Fixed energy intake: breakfast and preload

There were no differences in breakfast energy intake (25% of RMR) between conditions or MVPA groups (all $p>.05$). LoMVPA consumed 376.2 ± 48.4 kcal, ModMVPA consumed 395.9 ± 52.7 kcal, and HiMVPA consumed 409.7 ± 70.6 kcal on average during the three conditions.

By design, there was a significant effect of condition with regard to preload energy intake ($F(1.29,40.00)=319422.89$, $p<.001$), with post hoc analyses revealing that energy intake in the three conditions differed from each other (HEP: 687.9 ± 5.7 kcal vs. LEP: 254.0 ± 2.5 kcal vs. control: 0.0 kcal, $p<.001$).

5.3.3 Ad libitum energy intake - NEP

To assess baseline differences in energy intake between MVPA groups without a dietary manipulation, the NEP condition was at first analysed separately (Table 5-4). There were no significant differences between groups in energy intake at breakfast ($F(2,31)=1.06$, $p=.36$), lunch ($F(2,31)=1.23$, $p=.31$), dinner ($F(2,31)=1.95$, $p=.16$), evening snack box ($F(2,31)=0.07$, $p=.92$) or 24-h energy intake ($F(2,31)=1.23$, $p=.31$).

Table 5-4 Energy intake in the control NEP condition across groups of MVPA

	LoMVPA	**ModMVPA**	**HiMVPA**
Breakfast (kcal)	374.3 ± 51.5	395.5 ± 52.6	410.9 ± 73.2
Lunch (kcal)	828.9 ± 184.6	835.0 ± 252.9	972.3 ± 294.6
Dinner (kcal)	682.3 ± 183.7	635.0 ± 280.5	807.5 ± 176.3
Snack box (kcal)	586.5 ± 325.6	617.7 ± 309.7	633.1 ± 247.3
Daily energy intake (kcal)	2472.0 ± 603.9	2483.2 ± 649.6	2823.7 ± 596.5

5.3.4 Ad libitum energy intake - HEP and LEP

At lunch following consumption the LEP and HEP, LoMVPA consumed 523.6 ± 212.1 and 560.3 ± 224.3 kcal, ModMVPA 648.4 ± 390.3 and 440.3 ± 268.5 kcal and HiMVPA 812.9 ± 318.6 and 640.9 ± 267.2 kcal, respectively. Energy intake at lunch relative to NEP is presented in Figure 5-8. Analyses revealed a significant condition effect ($F(1,31)=8.79$, $p=.01$), as expected, with HEP suppressing subsequent energy intake to a greater degree than LEP. Furthermore, there was a significant interaction between condition and MVPA group ($F(2,31)=3.83$, $p=.03$). Post hoc analyses revealed that ModMVPA ($F(1,31)=9.41$, $p<.01$) and HiMVPA ($F(1,31)=7.01$, $p=.01$) had a greater reduction in intake relative to NEP after HEP compared to LEP, but no differences existed for LoMVPA ($F(1,31)=0.29$, $p=.59$). There was no significant main effect of MVPA group ($F(2,31)=1.88$, $p=.17$). There were no differences in water intake at lunch between conditions, MVPA group nor was there an interaction between the two (all $p>.05$).

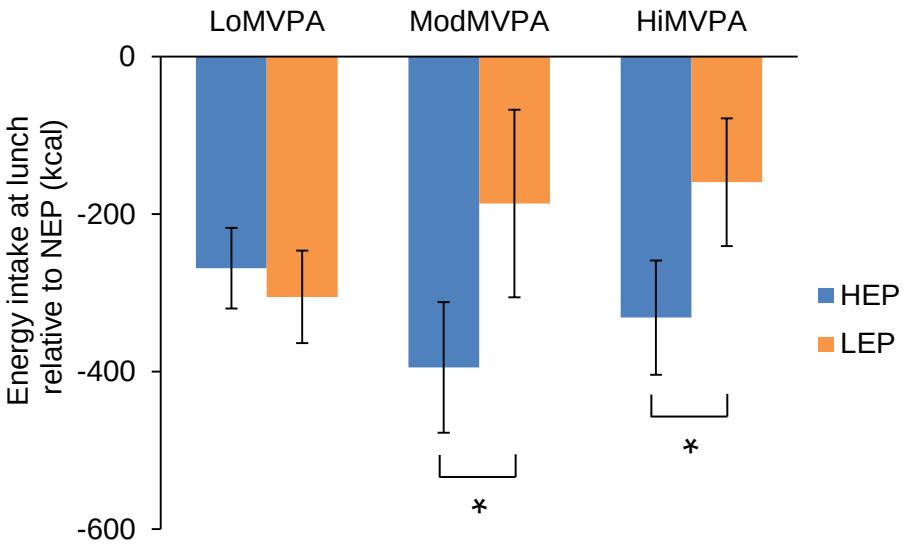

Figure 5-8 Energy intake at lunch after the HEP and LEP relative to control. *Post-hoc analyses showing difference between HEP and LEP ($p \leq .01$).

Absolute and relative energy intake at dinner, snack box and over 24 h are presented in Table 5-5. For relative energy intake at dinner or snack box, analyses demonstrated no significant main effect of condition (dinner: $F(1,31)=0.86$, $p=.36$; snack box: $F(1,31)=1.28$, $p=.27$) or MVPA group (dinner: $F(2,31)=1.13$, $p=.34$; snack box: $F(2,31)=0.65$, $p=.53$), or interaction between condition and MVPA group (dinner: $F(2,31)=0.74$, $p=.48$; snack box: $F(2,31)=1.75$, $p=.19$). In terms of total energy intake relative to NEP (including breakfast and preload), there was a significant effect of condition ($F(1,31)=43.81$, $p<.001$), with relative energy intake being greater in HEP compared to LEP, but there were no effect of MVPA group ($F(2,31)=0.37$, $p=.69$), or interaction between condition and MVPA group ($F(2,31)=2.45$, $p=.10$). There were no differences in water intake between conditions, MVPA groups nor was there an interaction between the two (all $p>.05$).

Table 5-5 Absolute and relative energy intake (kcal) at dinner, snack box and over 24h

	LoMVPA		ModMVPA		HiMVPA	
	LEP	**HEP**	**LEP**	**HEP**	**LEP**	**HEP**
Dinner	605.0 ± 224.2	635.4 ± 165.1	681.3 ± 253.6	663.6 ± 300.3	722.3 ± 235.6	791.0 ± 184.5
Δ Dinner	-77.3 ± 189.7	-46.9 ± 140.2	46.3 ± 233.9	28.6 ± 215.9	-85.2 ± 175.2	-16.4 ± 179.4
Snack box	501.0 ± 302.5	490.0 ± 332.5	579.7 ± 241.1	577.1 ± 321.1	543.9 ± 215.3	690.8 ± 320.0
Δ Snack box	-85.5 ± 93.4	-96.6 ± 194.6	-38.1 ± 217.3	-40.5 ± 178.9	-89.1 ± 191.1	57.7 ± 262.5
Daily EI	2260.3 ± 626.8	2751.5 ± 622.0	2559.5 ± 679.0	2764.7 ± 692.1	2741.7 ± 632.8	3220.3 ± 603.7
Δ Daily EI*	-211.7 ± 344.7	279.5 ± 430.8	76.3 ± 629.8	281.5 ± 493.4	-82.0 ± 352.9	396.6 ± 445.8

*Main effect of condition LEP vs. HEP $p<.001$. Δ, relative to NEP; *EI*, energy intake.

5.3.5 Compensation index

For COMPX at lunch following HEP and LEP, there were significant differences between groups (LoMVPA: -8.5 ± 37.6%, ModMVPA: 47.9 ± 51.6%, HiMVPA: 39.5 ± 61.8%; $F(2,33)=3.85$, $p=.03$), with post hoc analyses revealing that ModMVPA has significantly more accurate compensation than LoMVPA ($p=.047$). There were no differences between groups for COMPX calculated from lunch and dinner combined (LoMVPA: -15.5 ± 56.6%, ModMVPA: 51.8 ± 78.1%, HiMVPA: 23.7 ± 72.4%; $F(2,33)=2.59$, $p=.09$) or from lunch, dinner and snack box (LoMVPA: -12.8 ± 63.8%, ModMVPA: 52.9 ± 85.6%, HiMVPA: -9.9 ± 85.1%; $F(2,33)=2.46$, $p=.10$).

5.3.6 Subjective appetite ratings – NEP

Similarly to energy intake, to assess baseline and daily differences in appetite ratings between MVPA groups without a dietary manipulation, the NEP condition was at first analysed separately.

5.3.6.1 Hunger

Differences in baseline hunger ratings between MVPA groups approached significance (LoMVPA: 65.1 ± 17.0 mm, ModMVPA: 54.5 ± 19.5 mm, HiMVPA: 70.9 ± 13.0 mm; $F(2,31)=2.83$, $p=.07$). There were no differences in daily hunger between groups ($F(2,31)=1.04$, $p=.36$; Figure 5-9a).

5.3.6.2 Fullness

There were no significant differences between MVPA groups in baseline fullness ratings (LoMVPA: 12.0 ± 11.7 mm, ModMVPA: 20.2 ± 17.5 mm, HiMVPA: 12.0 ± 10.0 mm; $F(2,31)=1.39$, $p=.27$) or in daily fullness ($F(2,31)=0.26$, $p=.77$; Figure 5-9b).

5.3.6.3 Desire to eat

There were significant differences in baseline ratings of desire to eat between MVPA groups (LoMVPA: 69.3 ± 15.1 mm, ModMVPA: 56.8 ± 14.2 mm, HiMVPA: 76.8 ± 14.1 mm; $F(2,31)=5.53$, $p<.01$), with greater desire to eat in HiMVPA relative to ModMVPA ($p<.01$). There were no differences in daily desire to eat ($F(2,31)=2.60$, $p=.09$; Figure 5-9c).

5.3.6.4 Prospective food consumption

There were no significant differences in baseline ratings of PFC between MVPA groups (LoMVPA: 54.5 ± 17.0 mm, ModMVPA: 46.1 ± 22.5 mm, HiMVPA: 62.8 ± 14.9 mm; $F(2,31)=2.38$, $p=.11$) or in daily PFC ($F(2,31)=1.14$, $p=.33$; Figure 5-9d).

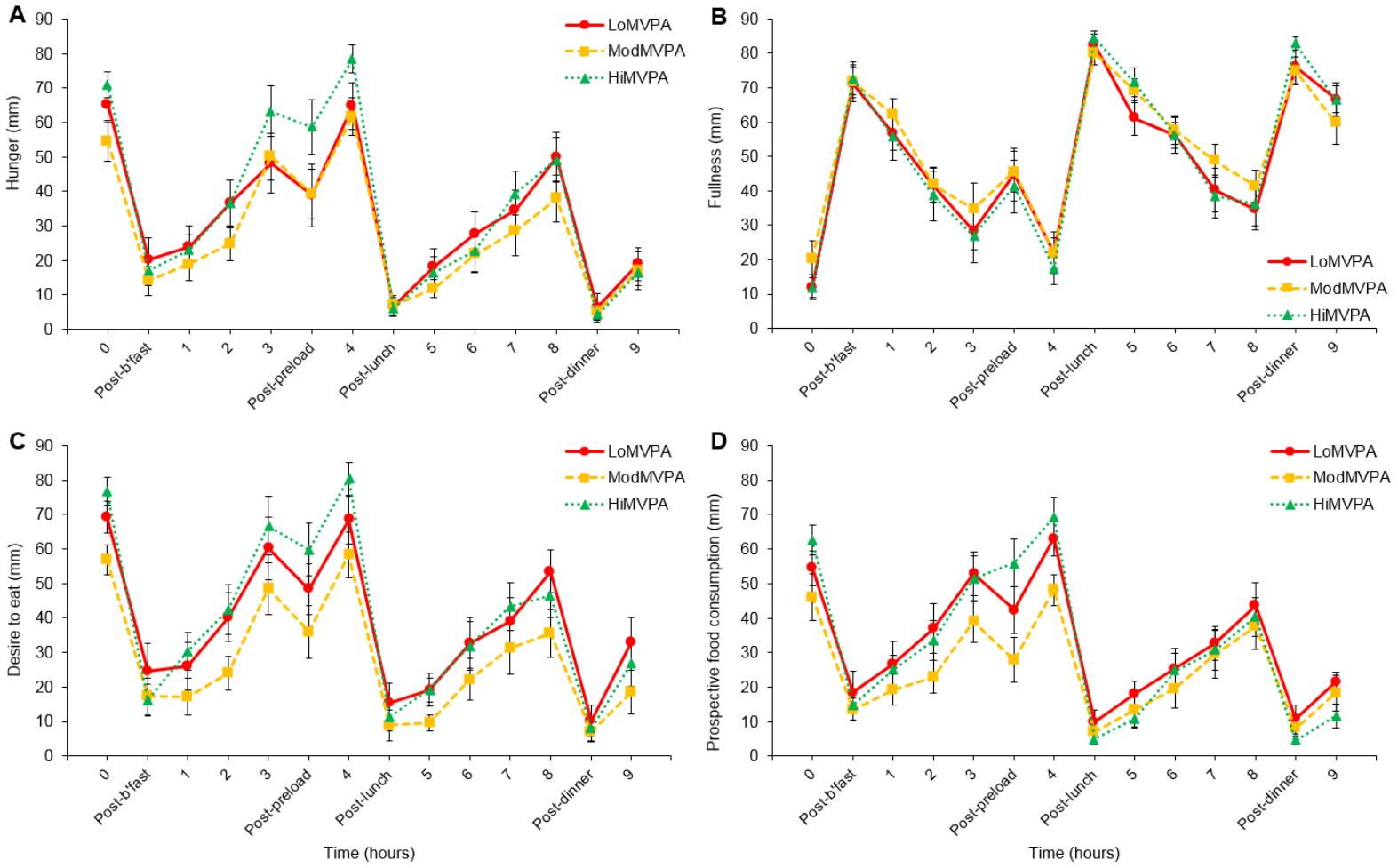

Figure 5-9 Daily profiles of hunger (A), fullness (B), desire to eat (C) and prospective food consumption (D) in NEP (water preload).

5.3.7 Subjective appetite ratings – HEP and LEP

The impact of the preloads on appetite sensations AUC relative to NEP was assessed over 1 h following preload consumption (post-preload) and over 2 h following preload and lunch consumption (post-preload and lunch). This is shown in Figure 5-10.

5.3.7.1 Hunger

Following preload consumption, there was a significant effect of condition (F(1,31)=5.23, p=.03), with hunger relative to NEP being more suppressed in HEP compared to LEP (Figure 5-10a). There was no main effect of MVPA group (F(2,31)=1.44, p=.25) or interaction between condition and MVPA group (F(2,31)=0.30, p=.74).

Following both preload and lunch consumption, there was a significant effect of condition (F(1,31)=5.24, p=.03), with hunger relative to NEP being more suppressed in HEP compared to LEP. There was no main effect of MVPA group (F(2,31)=0.29, p=.75) or interaction between condition and MVPA group (F(2,31)=0.41, p=.67).

5.3.7.2 Fullness

For fullness relative to NEP post-preload (Figure 5-10b), there was no significant effect of condition (F(1,31)=1.82, p=.19), MVPA group (F(2,31)=0.05, p=.95), or condition and MVPA group interaction (F(2,31)=0.17, p=.85).

Post-preload and lunch, there was a significant effect of condition (F(1,31)=6.69, p=.02), with fullness relative to NEP being greater in HEP compared to LEP. There was no main effect of MVPA group (F(2,31)=0.21, p=.81) or interaction between condition and MVPA group (F(2,31)=0.57, p=.57).

5.3.7.3 Desire to eat

For desire to eat relative to NEP post-preload (Figure 5-10c), there was no significant effect of condition (F(1,31)=0.54, p=.47), MVPA group (F(2,31)=1.34, p=.28), or condition and MVPA group interaction (F(2,31)=0.22, p=.80).

Post-preload and lunch, there was a significant effect of condition (F(1,31)=6.62, p=.02), with desire to eat relative to NEP being more suppressed in HEP compared to LEP. There was no main effect of MVPA group (F(2,31)=0.77, p=.47) or interaction between condition and MVPA group (F(2,31)=0.42, p=.67).

5.3.7.4 Prospective food consumption

For PFC post-preload (Figure 5-10d), there was no significant effect of condition (F(1,31)=0.06, p=.81), MVPA group (F(2,31)=1.51, p=.24), or condition and MVPA group interaction (F(2,31)=0.11, p=.90).

Post-preload and lunch, there was a significant effect of condition (F(1,31)=5.86, p=.02), with PFC relative to NEP being more suppressed in HEP compared to LEP. There was no main effect of MVPA group (F(2,31)=0.41, p=.67) or interaction between condition and MVPA group (F(2,31)=0.32, p=.73).

5.3.8 Satiety quotient

As shown in Table 5-6, SQ post-breakfast to pre-preload (0 to 3 h; 4 time points) revealed a significant effect of time (F(1.79,55.56)=75.68, p<.001), but no effect of MVPA group (F(2,31)=0.18, p=.84) or time and MVPA group interaction (F(3.59,55.58)=0.58, p=.66).

Table 5-6 Satiety quotient (SQ; mm/kcal) post-breakfast to 3 h

	LoMVPA	**ModMVPA**	**HiMVPA**
Post-breakfast	12.5 ± 5.0	11.3 ± 4.3	14.2 ± 5.2
1 h	10.4 ± 5.1	10.2 ± 4.8	11.5 ± 6.0
2 h	8.0 ± 4.8	7.6 ± 5.4	7.4 ± 6.3
3 h	1.1 ± 4.0	1.3 ± 5.3	1.2 ± 3.6

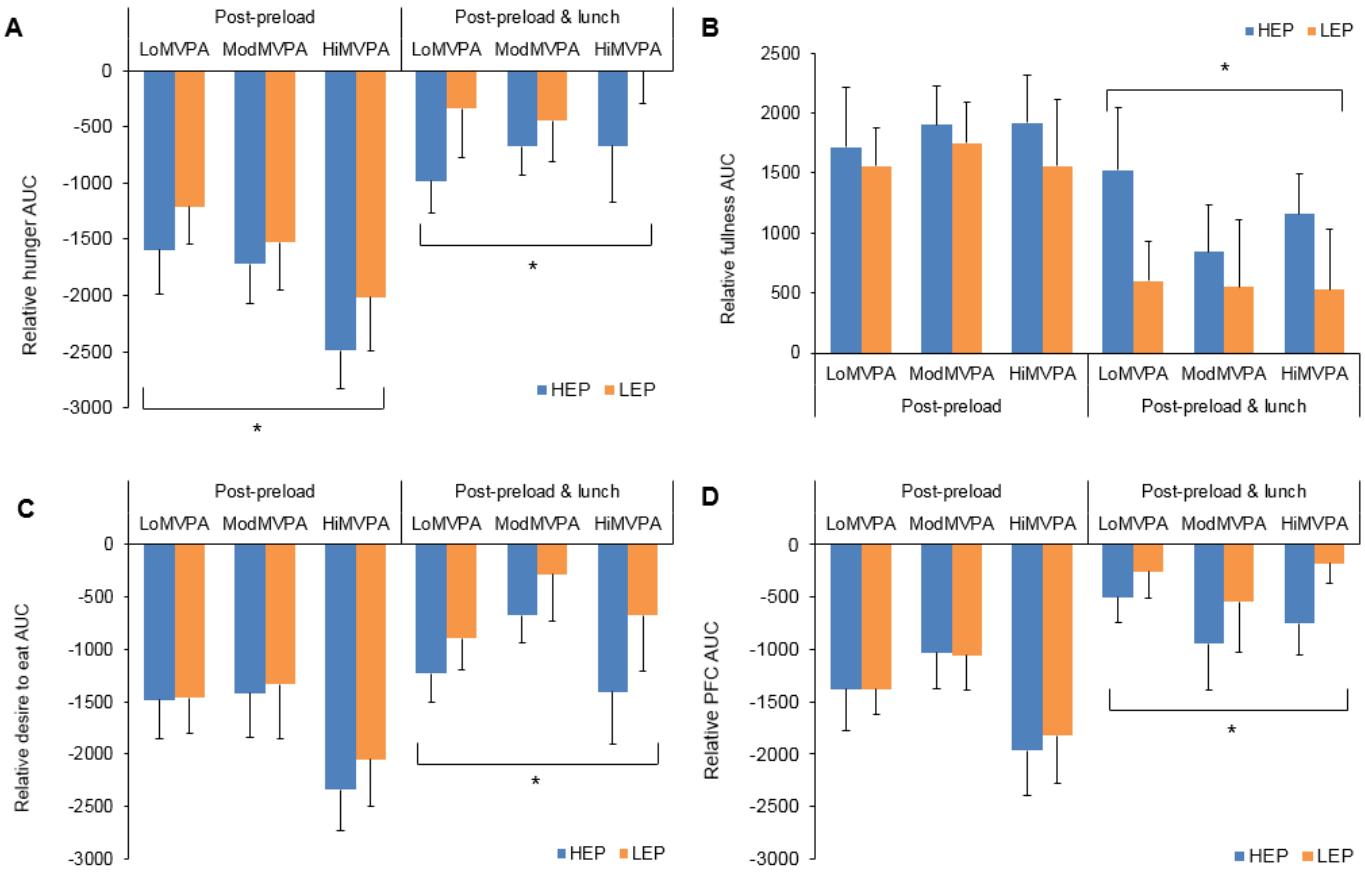

Figure Summary:

Post-preload: Greater suppression of hunger after HEP compared to LEP but no differences between groups.

Post-preload & lunch: Greater suppression of hunger, desire to eat and PFC, and greater fullness, after HEP compared to LEP but no differences between groups.

Figure 5-10 Hunger (A), fullness (B), desire to eat (C) and prospective food consumption (PFC; D) area under the curve (AUC) following HEP and LEP consumption relative to NEP. *Main effect of condition HEP vs. LEP $p<.05$.

5.3.9 Food reward – NEP

In the NEP condition, as expected, there were no differences in liking and wanting for high-fat relative to low-fat foods before or after water consumption or from pre- to post-water consumption (all p>.05; Table 5-7).

Table 5-7 Absolute liking and wanting pre- and post-preload consumption in the NEP condition

	LoMVPA	ModMVPA	HiMVPA[1]
Pre-Preload			
Liking	7.6 ± 18.7	3.4 ± 14.3	5.2 ± 19.2
Wanting	3.2 ± 32.2	6.1 ± 31.9	13.2 ± 40.5
Post-Preload			
Liking	8.4 ± 19.4	3.6 ± 13.4	4.6 ± 15.3
Wanting	12.8 ± 42.9	10.8 ± 31.6	11.9 ± 36.7

[1]n = 11.

5.3.10 Food reward – HEP and LEP

Absolute liking and wanting for high-fat relative to low-fat foods during HEP and LEP is presented in Table 5-8 and liking and wanting relative to NEP in Figure 5-11.

Table 5-8 Absolute liking and wanting pre- and post-consumption of preloads differing in energy content

	LoMVPA		ModMVPA		HiMVPA	
	LEP	HEP	LEP	HEP	LEP[1]	HEP
Pre-Preload						
Liking	6.2 ± 19.7	5.6 ± 13.3	-0.8 ± 16.8	3.8 ± 15.3	6.2 ± 13.6	6.2 ± 13.8
Wanting	1.9 ± 33.0	9.5 ± 32.6	1.5 ± 34.5	8.9 ± 35.0	15.9 ± 29.1	8.4 ± 37.4
Post-Preload						
Liking	4.5 ± 14.5	-3.6 ± 11.7	-5.0 ± 12.1	-0.2 ± 14.1	1.6 ± 9.0	-4.3 ± 16.0
Wanting	-2.0 ± 34.9	-12.3 ± 33.4	-22.2 ± 36.2	-23.4 ± 39.5	-2.8 ± 34.6	-14.3 ± 24.3

[1]n = 10.

Liking and wanting for high-fat relative to low-fat foods pre- and post-preload relative to NEP did not differ between conditions or MVPA groups, nor were there any condition and MVPA group interactions (p>.05 for all; Table 5-8).

For liking pre- to post-preload relative to control, there was a significant main effect of preload consumption (F(1,29)=7.32, p=.01), and condition and preload consumption interaction (F(1,29)=4.20, p=.05), with post hoc pairwise comparisons revealing a significant and greater reduction in liking pre- to post-preload after HEP (p<.01) compared with LEP (p=.10). There were no main effect of MVPA group, condition or other interaction effects (all p>.05; Figure 5-11a).

For wanting pre- to post-preload relative to control, there was a significant main effect of preload consumption (F(1,29)=20.48, p<.001) and condition and preload consumption interaction (F(1,29)=5.41, p=.03), with a greater reduction in wanting pre- to post-preload consumption after HEP (p<.001) compared to LEP (p=.001). There were no main effect of MVPA group, condition or other interaction effects (all p>.05; Figure 5-11b).

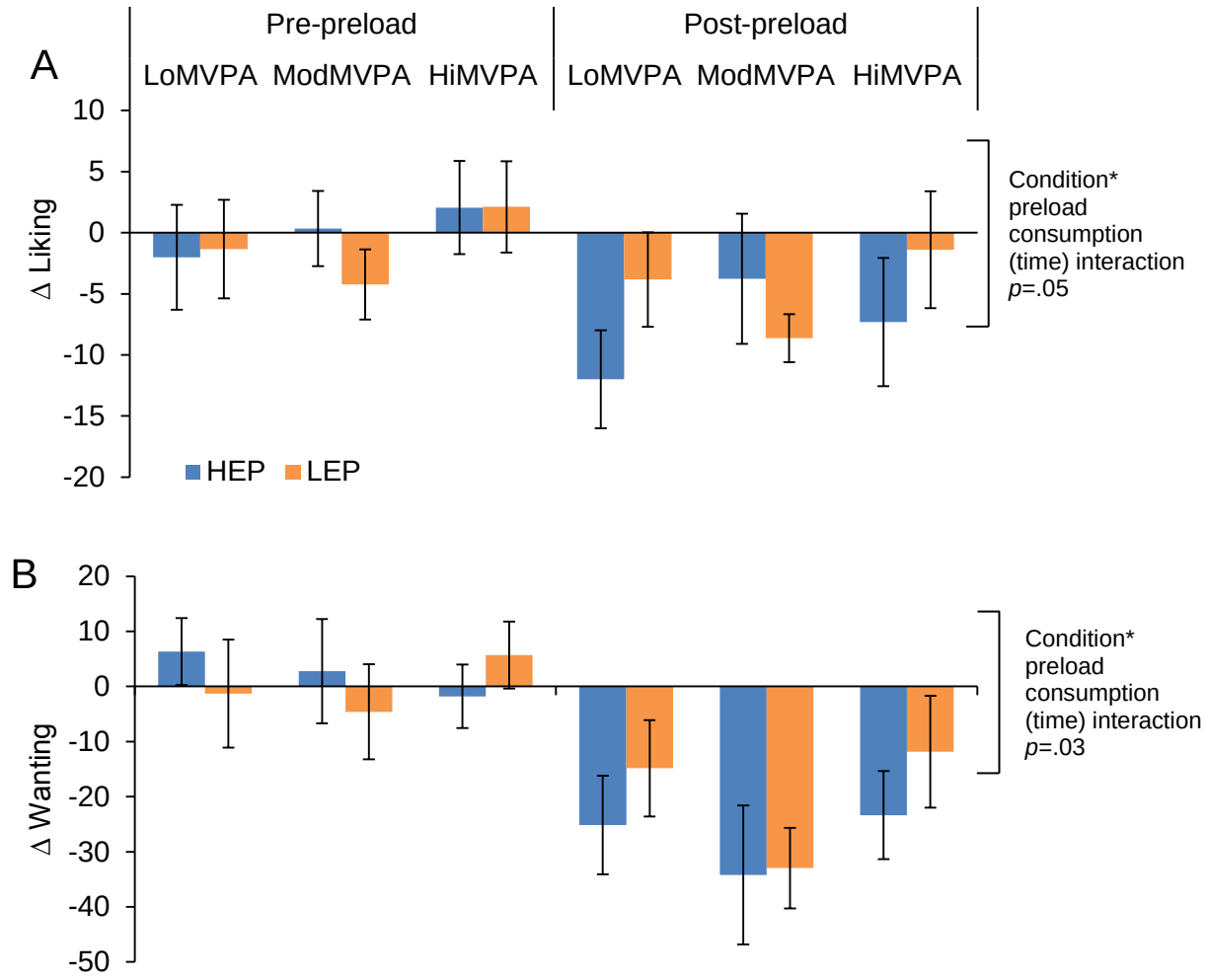

Figure 5-11 Liking (A) and wanting (B) relative to NEP (Δ) pre- and post-preload consumption. Condition and preload consumption (time) interaction showing greater suppression of liking and wanting following consumption of HEP compared to LEP.

5.3.11 Energy expenditure and energy balance

Energy expenditure did not differ significantly between meal days ($F(2,54)=0.12$, $p=.88$); therefore, only the NEP condition will be reported as energy intake in NEP was used for the energy balance analysis. SWA wear time (>18.5h) during the meal days was valid in 30 participants, and was not significantly different across groups. There were no differences in meal day energy expenditure (LoMVPA: 1964.6 ± 341.4 kcal; ModMVPA: 2077.0 ± 309.4 kcal; HiMVPA: 2270.4 ± 394.3 kcal; $F(2,27)=2.01$, $p=.15$) and meal day energy balance (energy intake – energy expenditure; LoMVPA: 507.4 ± 664.6 kcal; ModMVPA: 351.9 ± 762.8 kcal; HiMVPA: 423.8 ± 545.8 kcal; $F(2,27)=0.14$, $p=.87$). In all groups, meal day energy expenditure was significantly lower than habitual TDEE as measured by the SWA over 7 days ($p<.001$); therefore, energy balance was also calculated with TDEE (LoMVPA: 287.2 ± 558.6 kcal; ModMVPA: 47.8 ± 614.6 kcal; HiMVPA: 117.3 ± 587.6 kcal; $F(2,31)=0.49$, $p=.62$), and is shown in Figure 5-12 with the components of daily energy intake and expenditure.

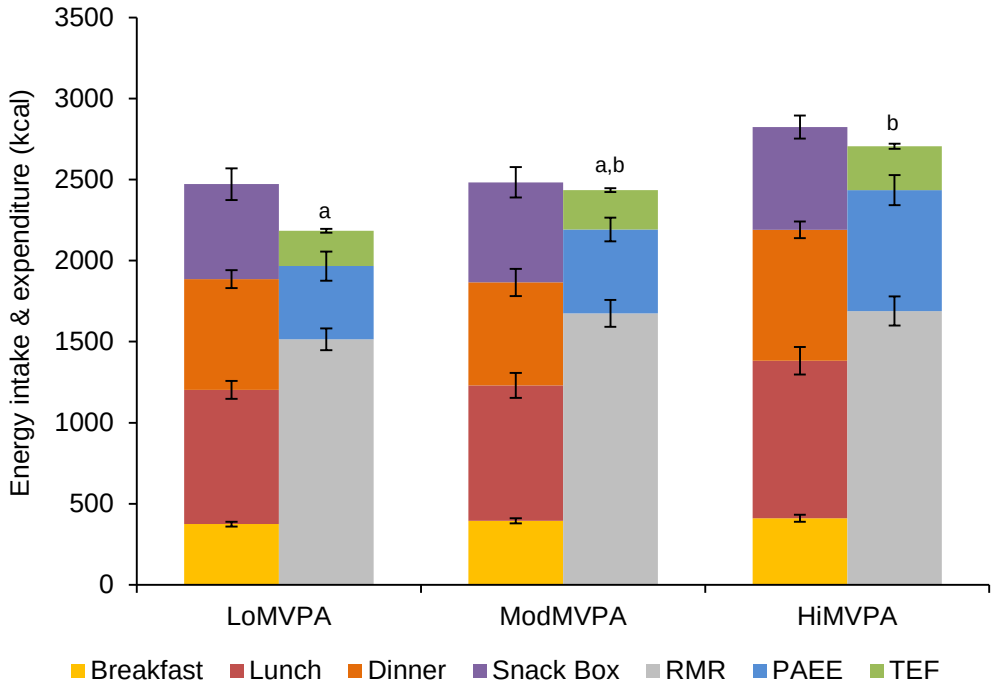

Figure 5-12 Components of daily energy intake in the NEP condition and habitual energy expenditure. Unalike letters indicate difference in total daily energy expenditure $p<.05$.

5.4 Discussion

This study investigated the strength of satiety, energy compensation and 24-h energy intake in individuals varying in physical activity levels using objective assessment of energy intake and habitual physical activity. Including the measurement of other biopsychological determinants of appetite control such as food reward allowed to examine their influence on satiety. In the entire sample, HEP gave rise to greater suppression of subsequent food intake than LEP. The HEP also led to a greater suppression of hunger and reduction in food reward (liking and wanting for high-fat foods) compared to the LEP across all MVPA groups. However, an examination of the different physical activity levels showed that ModMVPA and HiMVPA had a greater reduction of ad libitum energy intake at lunch following consumption of the HEP compared to the LEP, while LoMVPA did not, highlighting a role for habitual physical activity in the short-term sensitivity of appetite control.

5.4.1 Habitual physical activity and energy compensation

Unlike previous studies examining the impact of physical activity level on energy compensation, this study classified groups on objective and quantified habitual MVPA. Furthermore, to reduce the likelihood of confounding effects on the compensatory response, the preloads were matched for macronutrient composition and consisted of a semi-solid food (rather than a liquid), and participants were matched for age and BMI. The results show that the LoMVPA group were less sensitive to the nutritional manipulation of the preload, compared to the ModMVPA and HiMVPA groups who showed a greater reduction in intake in response to HEP. The poor compensatory response to the preload challenge in LoMVPA is also reflected by negative COMPX scores, indicative of greater consumption following HEP relative to LEP. This is suggestive of weakened short-term appetite sensitivity in the LoMVPA group, and is consistent with previous studies in which low levels of physical activity were found to be detrimental to homeostatic appetite control (Long et al., 2002; Martins et al., 2013; Martins, Truby, et al., 2007; Shook et al., 2015; Van Walleghen et al., 2007). In contrast, previous studies have reported that the physiological processes that signal satiety appear to be enhanced with habitual physical activity or exercise-training, with changes seen in postprandial appetite-related peptides favouring satiety (Guelfi et al., 2013; Lund et al., 2013; Martins et al., 2010; Martins et al., 2013). Interestingly, Sim et al. (2015) observed a tendency towards a reduction in energy intake following intake of a HEP (based on 95% confidence intervals) with a concomitant improvement in insulin sensitivity after 12 weeks of high-intensity intermittent exercise training but not

moderate-intensity continuous exercise training. This supports the thought that insulin (or leptin) sensitivity moderates the strength of satiety peptides such as CCK and GLP-1 (Morton et al., 2006; Schwartz et al., 2000; Verdich et al., 2001). Another process that could moderate the release of appetite-related peptides to signal satiety is gastric emptying, which was found to be faster in active compared to inactive males (Horner, Byrne, et al., 2015).

Thus, long-term habitual physical activity may lead to chronic physiological adaptations involved in satiety signalling, including improvements in body composition and insulin sensitivity, fine-tuning the appetite control system in its ability to detect adjustments in energy intake (over- or under-consumption) and to compensate appropriately at a subsequent meal. In line with these findings, the present study found intake to be reduced in the ModMVPA and HiMVPA groups in response to HEP. While improved post-meal satiety has been noted in physically active individuals, Chapter 4 reported that satiation does not differ between active and inactive individuals, as these distinct appetite processes may have differing underlying mechanisms (Beaulieu, Hopkins, et al., 2017a). Indeed, it is also possible that satiety is a more sensitive maker of homeostatic appetite control than satiation, as palatable (i.e. high-fat energy-dense) food can offset normal homeostatic appetite regulation and lead to hedonic or reward-related overconsumption (Blundell & Finlayson, 2004; Erlanson-Albertsson, 2005).

The acute preload response at the ad libitum lunch meal in ModMVPA and HiMVPA was similar to that previously observed (Long et al., 2002; Martins, Truby, et al., 2007; Sim et al., 2015). However, previous evidence on daily (cumulative) energy compensation is conflicting, with some studies demonstrating improvements in daily energy compensation with greater physical activity (Martins et al., 2013; Martins, Truby, et al., 2007) whereas another study, in line with the current results, suggests no improvements (Sim et al., 2015). Of note, assessment of daily energy intake in the aforementioned studies was done via food diaries which are prone to bias and misreporting, but in the current study, energy intake was objectively-assessed over 24 h. Other methodological factors may also explain these inconsistent findings, such as the different designs (exercise-training vs. cross-sectional), or physical characteristics (liquid vs. semi-solid) and macronutrient composition (matched vs. unmatched) of the preloads used between studies (Almiron-Roig et al., 2013). Nevertheless, total daily energy intake was greater following HEP compared to LEP in all MVPA groups. This highlights the importance of promoting the consumption of foods low in energy density to avoid a passive overconsumption of energy (Rolls, 2000), irrespective of physical activity level (Beaulieu, Hopkins, et al., 2017a).

5.4.2 Impact of HEP and LEP on appetite sensations and food reward

In all MVPA groups, compared to LEP, HEP consumption led to greater feelings of fullness and suppression of hunger, desire to eat and PFC following consumption of both the preload and lunch. Changes in appetite sensations following consumption of liquid preloads varying in energy content in inactive and active individuals have been inconsistent across studies, with one showing greater fullness after HEP compared to LEP (Martins, Morgan, Bloom, & Robertson, 2007), while others showing no differences in appetite sensations (Long et al., 2002; Martins et al., 2013). In the current study, a semi-solid preload was preferred over a liquid preload to elicit a strong impact on appetite and in the following compensatory response in energy intake within the time frame allocated between preload consumption and ad libitum meal (Almiron-Roig et al., 2003). Interestingly, all groups showed a greater suppression of hunger following HEP consumption but only the more active groups reduced energy intake at lunch after its consumption. As discussed above, the mechanisms which blunted the compensatory response in energy intake in LoMVPA remain to be fully elucidated.

To further assess satiety, changes in subjective hunger sensations relative to the energy content of the fixed breakfast via the SQ were examined, but were not influenced by MVPA group. Greater SQ values have been observed following 12 weeks of exercise-training in previously inactive overweight and obese individuals (Caudwell, Gibbons, Hopkins, Naslund, et al., 2013; King et al., 2009) suggesting improved satiety response to a fixed-energy meal. Differences in physical activity status (exercise-training intervention vs. habitual physical activity) and also in weight status of the participants (lean vs. overweight and obese) could explain these contradictory findings.

The consumption of the HEP was reflected by a greater reduction in both liking and wanting relative to LEP, without any differences between groups. This reduction in food reward was likely mediated by the greater energy content of the HEP (~440 kcal) and subsequent greater suppression of hunger following its consumption. In contrast, there were no significant differences in liking and wanting in Chapter 4 following ad libitum consumption of a high-fat/high-energy-dense meal compared to a low-fat/low-energy-dense meal (to a similar level of fullness) despite a greater energy intake of just below 400 kcal at the high-fat meal (Beaulieu, Hopkins, et al., 2017a). Thus, it appears that an individual's hunger/satiety state may mediate the food reward response to meals to a greater extent than energy content or macronutrient composition, with greater suppression of hunger and perceived fullness leading to a greater reduction in liking and wanting for high-fat relative to low-fat foods.

Alternatively, consumption of fixed (i.e. preload) and ad libitum meals may produce distinct responses in food reward.

While the energy content of the preloads used in the current study varied, their macronutrient composition was matched to control for any nutrient-specific effects; however, it is known that per calorie consumed, carbohydrates influence satiety to a greater degree than fat (Blundell, Burley, Cotton, & Lawton, 1993). Indeed, Hopkins et al. (2016) observed a greater reduction in liking and wanting for high-fat foods and a greater suppression of hunger (via the SQ) following consumption of a low-fat compared to a high-fat isoenergetic meal in inactive overweight and obese individuals. As such, choosing low-fat/low-energy dense foods to promote greater satiety could not only reduce the perceived hedonic value of food in the fed state but also be less likely to lead to an increase in energy intake.

In terms of the influence of physical activity level on food reward, in the current non-obese sample, no differences in food reward among MVPA groups were observed. These findings are similar to the previous study in Chapter 4 where similarities in food reward in non-obese individuals with high or low levels of physical activity were also found (Beaulieu, Hopkins, et al., 2017a). Heightened food reward may be dependent upon a greater accumulation of body fat, as greater liking and wanting for high-fat foods have been observed in overweight inactive males compared to their leaner active counterparts (Horner et al., 2016) and also in overweight/obese females compared to healthy-weight females (Nijs, Muris, Euser, & Franken, 2010).

5.4.3 Impact of physical activity level on daily energy intake and appetite sensations

Without the dietary manipulation of the preload, in the NEP condition, daily energy intake was not significantly different between MVPA groups, despite intake being 350 kcal greater in HiMVPA relative to LoMVPA (*d*=0.59). However, the data follow a similar trend as a study by Tucker (2016) in which self-reported energy intake increased across quartiles of measured habitual physical activity in 300 middle-aged women with a mean BMI of 24 kg/m^2. In that study, women with high levels of physical activity consumed 171 kcal more per day than those with low levels of physical activity. These data suggest a linear relationship between physical activity level and energy intake in non-obese individuals. Indeed, in non-obese individuals ranging from low to high levels of physical activity such as in the current study, this fits within the right-hand side of the J-shape relationship observed by Mayer et al. (1956), where energy intake increases according to physical activity level. The left-hand side of this

relationship would be characterised by very inactive/sedentary individuals with overweight and obesity. The relationships among measures of habitual physical and energy intake will be further examined and discussed in the following chapter.

Likewise, HiMVPA had a greater fasting ratings of desire to eat (and a tendency towards greater hunger), corroborating data from Harrington et al. (2013) that revealed greater fasting appetite with increasing levels of habitual physical activity. Intervention studies also found an increase in fasting hunger (Caudwell, Gibbons, Hopkins, King, et al., 2013; King et al., 2009; Martins et al., 2010), desire to eat and PFC (Martins et al., 2010) following 12 weeks of exercise-training. This greater drive to eat with high levels of physical activity likely stems from increased daily energy needs but also from metabolic requirements derived from fat-free mass. This raises the question of whether physical activity per se drives energy intake. This will be addressed in the following chapter.

5.4.4 Limitations

A strength of this study was that it included an objective assessment of habitual physical activity to classify groups according to measured MVPA and the inclusion of probe meal days to quantify 24-h energy intake. However, despite energy intake being measured in well-controlled conditions, this may not have reflected ‘real-world’ or long-term effects. Furthermore, this enhanced control did not allow for a very large sample size. Assessment of postprandial appetite-related peptides following the preloads could also have provided a better depiction of homeostatic satiety signalling differences between the MVPA groups, and should be addressed in future studies. It should also be noted that the study only included non-obese individuals and this did not allow for the inclusion of very inactive and sedentary individuals; therefore, the individuals in the LoMVPA group were relatively active. Consequently, any inferences of enhanced homeostatic appetite control with higher levels of physical activity should not be made for obese individuals.

5.4.5 Conclusions

Consumption of a HEP reduced energy intake at the following meal in non-obese individuals with moderate to high levels of MVPA relative to a LEP, but this effect was absent in individuals with low levels of MVPA. This suggests individuals with low levels of physical activity have weaker satiety response to food and fail to discriminate between the different energy contents of the preloads. On the other hand, individuals who are more physically active are sensitive to the energy content of foods and have

better ability to adjust energy intake at a subsequent meal. The mechanisms underlying this process remains to be fully elucidated, but could be linked to homeostatic rather than hedonic mechanisms. Using rigorous measures of physical activity and energy intake, these data provide objective support to previous evidence that low levels of physical activity are detrimental to acute homeostatic appetite control. This weaker compensatory response in individuals with low levels of physical activity, coupled with a lower daily energy expenditure, leaves them vulnerable to positive energy balance and weight gain in the long-term.

Chapter summary:

- ModMVPA and HiMVPA reduced ad libitum energy intake at the lunch meal following consumption of a HEP compared to a LEP, while LoMVPA did not.
- In all MVPA groups, consumption of the HEP induced a greater suppression of hunger and hedonic preference for high-fat foods than LEP.
- HiMVPA was characterised with a greater fasting desire to eat and greater energy intake.
- These objective data provide confirmatory evidence that habitual physical activity is associated with enhanced short-term homeostatic appetite control, potentially mediated by physiological satiety signalling.

Chapter 6 – Associations among components of physical activity, energy expenditure, energy intake and appetite control (PALACE – Physical Activity Level, Appetite Control and Energy balance)

Chapter aims:

- Examine the associations between components of physical activity (time spent in light, moderate and vigorous physical activity, PAEE, VO_{2max} and PAL), meal size and daily energy intake.
- Determine the strongest predictor of energy intake among measures of physical activity, body composition and energy expenditure.
- Investigate the relationships among components of physical activity and determinants of appetite control (appetite sensations, satiety quotient, body composition, fasting appetite-related peptides, eating behaviour traits and food reward).

6.1 Introduction

Classic energy balance studies have provided initial evidence for the inter-relationships between energy expenditure and energy intake. For example, Edholm et al. demonstrated that energy expenditure and energy intake were not well correlated over a single day, but over three weeks the correlation was strong (Edholm et al., 1970; Edholm et al., 1955). Years later, a role for energy expenditure as a driver of energy intake was proposed (Blundell et al., 2001). Several studies have now supported this proposition, having found significant associations between hunger, energy intake and energy expenditure (including RMR and TDEE), and also with fat-free mass, a large determinant of energy expenditure (Blundell et al., 2012a; Caudwell, Finlayson, et al., 2013; Cugini et al., 1998; Hopkins, Finlayson, et al., 2016; Lissner et al., 1989; McNeil et al., 2017; Piaggi et al., 2015; Weise et al., 2014). Because RMR contributes to approximately 60% of TDEE, it has been hypothesised that it provides a tonic signal of hunger and energy intake (Blundell, Finlayson, et al., 2015). Whereas RMR remains relatively constant on a day-to-day basis, physical

activity is quite a volatile component of the energy expenditure budget, and whether it contributes to the drive to eat is not well understood.

Earlier views suggested a loose coupling between physical activity and energy intake (Blundell & King, 1998) and, more recently, a systematic review did not find convincing evidence that physical activity or exercise leads to an increase in energy intake (Donnelly et al., 2014). However, most studies were relatively short-term and may not have been long enough to demonstrate a compensatory rise in energy intake. Furthermore, the relationship between physical activity level and energy intake may not be linear and might differ between individuals varying in weight status. This was initially demonstrated by Mayer et al. (1956) with a J-shape relationship between daily physical activity level and daily energy intake, where a positive linear relationship between physical activity level and energy intake existed, but only in those with higher levels of daily physical activity and lowest body weight. This relationship between physical activity level and energy intake has recently been replicated in the systematic review in Chapter 2 (Beaulieu et al., 2016) and in a study using an equation based on changes in body composition to indirectly estimate energy intake (Shook et al., 2015). These data are in line with Tucker (2016), who found that 7-day objectively measured physical activity in 300 women (mean BMI of 24 kg/m^2) was significantly positively associated with self-reported energy intake over those days. Taken together, these studies suggest that within a healthy/non-obese range of body weight (i.e. within the right-hand side of the J-shape relationship), an increase in habitual physical activity leads to higher energy intake; however, they were not based on objective measures of both physical activity and energy intake. Moreover, the impact of the several components of habitual physical activity (e.g. cardiorespiratory fitness, minutes at various intensities of physical activity and PAEE) on energy intake and appetite control remains unknown.

The above evidence suggests an excitatory source driving food intake, but the adipocentric view of appetite regulation proposes that fat mass exerts an inhibitory effect on food intake, via tonic signals stemming from insulin and leptin (Morton et al., 2006). In addition, it has been proposed that the inhibitory effect of fat mass is weakened as levels of body fat increase as a consequence of central and peripheral insulin and leptin resistance, providing a justification as to why overweight and obese individuals continue to be hungry and overconsume despite having excessive amounts of body fat (Blundell, Finlayson, et al., 2015). Indeed, in individuals with an average BMI of 22 kg/m^2, a significant negative relationship between fat mass and energy intake was found, but this relationship was absent in overweight and obese individuals with an average BMI of approximately 31 kg/m^2 (Blundell et al., 2012a; Blundell,

Finlayson, et al., 2015). These findings corroborate prior associations found between hunger and body composition (positive with fat-free mass and negative with fat mass) in lean but not obese individuals (Cugini et al., 1999; Cugini et al., 1998). Whether physical activity influences the relationship between fat mass and energy intake is unknown. Given that habitual physical activity improves insulin sensitivity (Goodyear & Kahn, 1998) and insulin sensitivity may be involved in the strength of episodic satiety signalling (Flint et al., 2007; Speechly & Buffenstein, 2000), physical activity may moderate the relationship between fat mass and energy intake.

6.1.1 Objectives

The purpose of this study was to explore whether specific components of objectively-assessed physical activity, body composition or energy expenditure were associated with measured meal size and daily energy intake, and with homeostatic and hedonic determinants of appetite control. For this investigation, data obtained from the two previous studies (Chapters 4 and 5) were combined and the following measures/components of physical activity were examined: time spent in light, moderate and vigorous physical activity, PAEE, VO_{2max} and PAL. Specifically, the analyses sought to test the following hypotheses in non-obese and relatively active individuals: 1) habitual physical activity is associated with energy intake, but considering the other contributors to energy expenditure, is not the strongest predictor of energy intake; and 2) the strength of the association between fat mass and energy intake will vary with the level of physical activity.

6.2 Methods

6.2.1 Participants

Participants were recruited, and ethical approval and written informed consent were obtained as described in Chapters 4 and 5. Briefly, 70 adults aged 18-55 years were screened for inclusion based on the following criteria: BMI <30 kg/m^2, non-smoker, weight stable (±2 kg for previous 3 months), not currently dieting, not taking any medication known to affect metabolism or appetite, and acceptable ratings of the study foods. The included participants all provided valid SWA data (>22 h of verifiable time per day for at least 5 days, including 1 weekend day; Chapter 4 *n*=36 and Chapter 5 *n*=34).

6.2.2 Study design

Data obtained from the studies in Chapters 4 and 5 were combined for these secondary analyses to examine associations between different components of physical activity and appetite control in non-obese and relatively active individuals. All participants completed a similar preliminary assessment where body composition, eating behaviour traits, RMR, VO_{2max}, and fasting appetite-related peptides (Chapter 4 only) were assessed, followed by meal days where meal size and daily energy intake (Chapter 5 only) were determined.

6.2.3 Preliminary assessment

During the preliminary assessment, body composition (fat mass and fat-free mass), RMR, eating behaviour traits (TFEQ, BES, CoEQ) and VO_{2max} were assessed as described in Chapter 3. Fasted appetite-related peptides were collected in a subsample as described in Chapter 4 (glucose *n*=36, insulin *n*=36, leptin *n*=36, and acylated ghrelin *n*=22).

6.2.4 Free-living energy expenditure and physical activity

Free-living TDEE, PAL, and minutes in light, moderate and vigorous physical activity were obtained from the SWA software as described in Chapter 3. PAEE was calculated by subtracting measured RMR and estimated thermic effect of food (~10% of TDEE) following the equation PAEE = 0.9TDEE – RMR (Westerterp, 2004).

6.2.5 Meal size and 24-h energy intake

Energy intake at lunch in the HCHO condition from Chapter 4 and in the control condition from Chapter 5 were used for the analysis of meal size. By design, the meals differed significantly in energy density and macronutrient composition (Table 6-1); thus, in all meal size analyses, the study was a covariate. To extend the associations to daily energy intake, total daily energy intake in the control condition from Chapter 5 was included in a subsample (*n*=34).

Table 6-1 Meal characteristics

Study	Chapter 4 COMPAS	Chapter 5 SCOPE	*P*-value
Meal size (kcal)	1016.6 ± 291.6	881.45 ± 251.6	**.04**
Meal size (g)	735.0 ± 211.9	715.2 ± 187.8	.68
Energy density (kcal/g)	1.38 ± 0.03	1.23 ± 0.14	**<.001**
% carbohydrate	70.8 ± 0.01	53.3 ± 0.08	**<.001**
% fat	21.9 ± 0.21	39.6 ± 0.18	**<.001**
% protein	8.7 ± 0.2	7.1 ± 0.18	**<.001**
Daily energy intake (kcal)	-	2599.7 ± 620.6	

6.2.6 Appetite sensations and satiety quotient

Fasting and morning AUC (over 3h using the trapezoid method) ratings of hunger, fullness, desire to eat and PFC were used as described in Chapter 3. The SQ was calculated as described in Chapter 3 using the average of the four hunger ratings following breakfast consumption and energy intake at breakfast. Energy intake at breakfast across studies was similar (Chapter 4: 422.1 ± 169.5 kcal and Chapter 5: 394.1 ± 60.5 kcal; $t(44.23)=.93$, $p=.36$) and accounted for 25.9 ± 9.4 % of RMR in Chapter 4 and 24.4 ± 2.0 % of RMR in Chapter 5.

6.2.7 Food reward

Because of the dietary manipulation differences between the studies, only the scores in the hungry state (Chapter 4: 4h post-breakfast; Chapter 5: 3h post-breakfast) from the LFPQ were included in the analysis. Fat appeal bias scores (preference for high-fat relative to low-fat foods) were computed for both implicit wanting and explicit liking as described in Chapter 3.

6.2.8 Statistical analysis

Pearson's correlations and partial correlations, controlling for a third variable such as study, sex, TDEE and body composition (where appropriate) were conducted to assess relationships among variables. Multiple stepwise regression was performed to determine the strongest predictor of meal size. To examine the effects of physical activity level in the relationship between body composition and meal size, participants were grouped by sex-specific tertiles of measured daily MVPA (low: LoMVPA, moderate: ModMVPA, or high: HiMVPA) obtained from the SWA. For males, LoMVPA

corresponded to <112 min MVPA/day and HiMVPA to >167 min MVPA/day, while for females, LoMVPA corresponded to <92 min MVPA/day and HiMVPA to >147 min MVPA/day. One-way ANOVAs were used to determine differences between groups and partial correlations, controlling for study, were conducted to assess the strength of the associations between body composition and meal size at different physical activity levels.

6.3 Results

6.3.1 Participant characteristics and inter-correlations

The participant characteristics for body composition, VO_{2max}, eating behaviour traits and fasted appetite-related peptides are shown in Table 6-2. Individual variability in RMR, PAEE and TDEE is illustrated in Figure 6-1. RMR represented 64.6 ± 9.2 % (range 47-85%) of TDEE and PAEE represented 25.4 ± 9.2 % (range 5-43%) of TDEE. The remaining 10% was represented by TEF.

RMR was positively associated with fat-free mass ($r(68)= .71$, $p<.001$), VO_{2max} ($r(67)= .45$, $p<.001$), PAL ($r(68)= .35$, $p=.003$), moderate PA ($r(68)= .27$, $p=.02$), vigorous PA ($r(68)= .28$, $p=.02$), MVPA ($r(68)= .31$, $p=.009$), and total PA ($r(68)= .27$, $p=.03$), and negatively associated with percentage body fat ($r(68)= -.42$, $p<.001$) but not associated with light PA or fat mass. Only the associations with fat-free mass, VO_{2max}, PAL, moderate PA and MVPA remained significant when controlling for sex (all $p<.04$).

PAEE was positively associated with fat-free mass ($r(68)= .65$, $p<.001$), RMR ($r(68)= .25$, $p=.04$), VO_{2max} ($r(67)= .61$, $p<.001$), PAL ($r(68)= .73$, $p<.001$), light PA ($r(68)= .47$, $p<.001$), moderate PA ($r(68)= .55$, $p<.001$), vigorous PA ($r(68)= .66$, $p<.001$), MVPA ($r(68)= .67$, $p<.001$), and total PA ($r(68)= .63$, $p<.001$), and negatively associated with fat mass ($r(68)= -.30$, $p=.01$) and percentage body fat ($r(68)= -.52$, $p<.001$). Only the association with fat mass did not remain significant when controlling for sex.

TDEE was positively associated with fat-free mass ($r(68)= .85$, $p<.001$), RMR ($r(68)= .72$, $p<.001$), PAEE ($r(68)= .85$, $p<.001$), VO_{2max} ($r(67)= .68$, $p<.001$), PAL ($r(68)= .71$, $p<.001$), light PA ($r(68)= .44$, $p<.001$), moderate PA ($r(68)= .54$, $p<.001$), vigorous PA ($r(68)= .62$, $p<.001$), MVPA ($r(68)= .65$, $p<.001$) and total PA ($r(68)= .60$, $p<.001$), and negatively associated with fat mass ($r(68)= -.28$, $p=.02$) and percentage body fat ($r(68)= -.60$, $p<.001$). When controlling for sex, these associations remained highly significant (all $p\leq.002$), except for fat mass which did not remain significant.

Table 6-2 Descriptive statistics of study sample

	Mean ± SD (range)
N	70 (61% F)
Age (years)	29.5 ± 9.1 (19.0 - 53.0)
Body mass index ($kg \bullet m^{-2}$)	22.7 ± 2.3 (19.5 - 29.2)
Total mass (kg)	65.7 ± 10.8 (48.8 - 92.6)
Fat mass (kg)	15.5 ± 5.4 (3.8 - 28.6)
Fat-free mass (kg)	50.2 ± 10.9 (34.7 - 78.4)
Body fat (%)	23.9 ± 7.9 (5.3 - 39.7)
RMR ($kcal \bullet 24h^{-1}$)	1628.8 ± 267.3 (1086.1 - 2226.8)
VO_{2max} ($mL \bullet kg^{-1} \bullet min^{-1}$)	42.8 ± 9.2 (24.1 - 63.2)[1]
TDEE ($kcal \bullet day^{-1}$)	2570.7 ± 550.7 (1746.7 - 3815.8)
PAEE ($kcal \bullet day^{-1}$)	684.8 ± 355.3 (102.8 - 1578.5)
Light PA ($min \bullet day^{-1}$)	262.2 ± 83.6 (78.2 - 462.6)
Moderate PA ($min \bullet day^{-1}$)	106.8 ± 39.4 (46.1 - 214.5)
Vigorous PA ($min \bullet day^{-1}$)	29.4 ± 26.6 (0.4 - 108.3)
MVPA ($min \bullet day^{-1}$)	136.2 ± 58.4 (8.8 - 275.3)
Total PA ($min \bullet day^{-1}$)	398.4 ± 124.5 (127.0 - 699.7)
PAL	1.68 ± 0.22 (1.28 - 2.30)
Daily steps	10083.6 ± 3385.8 (2930.4 - 18680.7)
Restraint	7.7 ± 4.5 (0.0 - 18.0)
Disinhibition	5.8 ± 3.2 (1.0 - 15.0)
Binge eating score	8.4 ± 6.5 (0.0 - 27.0)
Craving control	60.3 ± 20.0 (22.8 - 97.8)

[1] *n*=69.

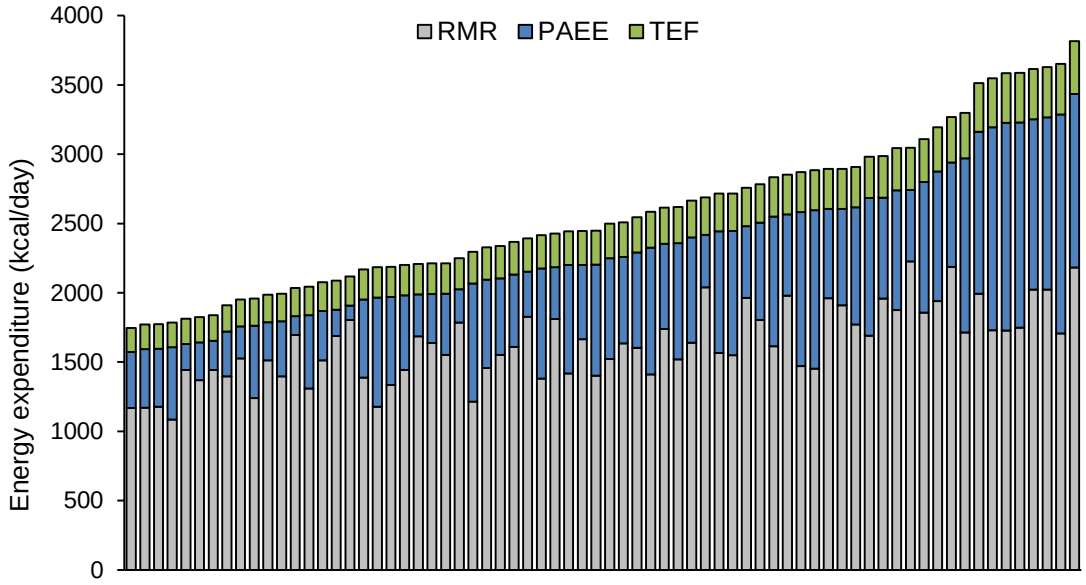

Figure 6-1 Individual profile of the components of daily energy expenditure including resting metabolic rate (RMR), physical activity energy expenditure (PAEE), thermic effect of food (TEF).

6.3.2 Associations between physical activity and body composition

As shown in Table 6-3, physical activity was associated with several markers of body composition, demonstrating clear negative correlations between most components of physical activity and fat mass and body fat percentage, even after controlling for sex. Fewer components of physical activity were associated with fat-free mass; these included VO_{2max}, PAEE, PAL, vigorous physical activity and total physical activity, but the two latter did not remain significant after controlling for sex.

Table 6-3 Correlations between components of habitual physical activity and body composition

	Total mass (kg)	**Fat mass (kg)**	**Fat-free mass (kg)**	**Body fat (%)**	**BMI ($kg \bullet m^{-2}$)**
VO_{2max} ($mL \bullet kg^{-1} \bullet min^{-1}$)[1]	**.273***	**-.564*****	**.551*****	**-.677*****	-.078
PAEE ($kcal \bullet day^{-1}$)	**.503*****	**-.299***	**.647*****	**-.521*****	.177
PAL	.127	**-.371****	**.309****	**-.438*****	-.150
Light PA ($min \bullet day^{-1}$)	-.064	**-.598*****	.231	**-.581*****	**-.302***
Moderate PA ($min \bullet day^{-1}$)	.019	**-.295***	.165	**-.297***	-.166
Vigorous PA ($min \bullet day^{-1}$)	-.019	**-.549*****	**.252***	**-.550*****	**-.295***
MVPA ($min \bullet day^{-1}$)	.004	**-.449*****	.226	**-.451*****	**-.247***
Total PA ($min \bullet day^{-1}$)	-.041	**-.612*****	**.261***	**-.602*****	**-.318****
Controlling for sex					
VO_{2max} ($mL \bullet kg^{-1} \bullet min^{-1}$)[1]	.012	**-.501*****	**.413*****	**-.593*****	-.231
PAEE ($kcal \bullet day^{-1}$)	.228	-.153	**.411*****	**-.275***	.012
PAL	.012	**-.336****	**.280***	**-.421*****	-.219
Light PA ($min \bullet day^{-1}$)	**-.328****	**-.560*****	.025	**-.547*****	**-.419*****
Moderate PA ($min \bullet day^{-1}$)	-.024	**-.293***	.201	**-.334****	-.193
Vigorous PA ($min \bullet day^{-1}$)	**-.309***	**-.498*****	.000	**-.478*****	**-.431****
MVPA ($min \bullet day^{-1}$)	-.153	**-.420*****	.138	**-.439*****	**-.322****
Total PA ($min \bullet day^{-1}$)	**-.293***	**-.577*****	.083	**-.577*****	**-.435*****

[1]*n*=69. **p*<.05; ***p*<.01; ****p*<.001.

6.3.3 Associations between components of physical activity and energy intake

As shown in Table 6-4, after controlling for study, meal size was significantly associated with all components of physical activity except for light PA. The associations with VO_{2max}, PAEE, PAL, moderate PA and MVPA remained significant after controlling for sex, but none of the associations remained significant after controlling for TDEE.

To extend on the findings obtained for meal size, a subsample analysis (*n*=34) was performed to examine associations between the aforementioned parameters, and daily (24-h) energy intake. The only significant associations with the components of

physical activity were with VO_{2max} (r(31)= .50; p=.003) and vigorous PA (r(32)= .35; p=.045). The associations with total PA (r(32)= .33; p=.057) and MVPA (r(32)= .31; p=.075) approached significance. Only the association with VO_{2max} remained significant after also controlling for sex (r(30)= .36; p=.04).

Table 6-4 Associations between components of physical activity and meal size

	Meal size (kcal)[1]	**Meal size (kcal)[2]**
VO_{2max} ($mL \bullet kg^{-1} \bullet min^{-1}$)[3]	**.361****	**.245***
PAEE ($kcal \bullet day^{-1}$)	**.424*****	**.289***
PAL	**.339****	**.309***
Light PA ($min \bullet day^{-1}$)	.223	.142
Moderate PA ($min \bullet day^{-1}$)	**.277***	**.279***
Vigorous PA ($min \bullet day^{-1}$)	**.256***	.169
MVPA ($min \bullet day^{-1}$)	**.303***	**.266***
Total PA ($min \bullet day^{-1}$)	**.293***	.223

[1]Controlling for study; [2]Controlling for study and sex; [3]n=69. *p<.05; **p<.01; ***p<.001.

6.3.4 Associations between body composition, other components of energy expenditure and energy intake

As shown in Table 6-5, after controlling for study, meal size was significantly associated with total mass, fat mass, fat-free mass, percentage body fat, RMR and TDEE. Only the associations with fat-free mass and TDEE remained significant after also controlling for sex.

Daily energy intake was associated with fat mass (r(32)= -.50, p=.002), fat-free mass (r(32)= .51, p=.002), percentage body fat (r(32)= -.60, p<.001), RMR (r(32)= .53, p=.001) and TDEE (r(32)= .48, p=.004), but not with total mass or BMI. After controlling for sex, daily energy intake remained associated with fat mass (r(31)= -.41, p=.02) and percentage body fat (r(31)= -.39, p=.03).

Table 6-5 Associations among body composition, energy expenditure and meal size

	Meal size (kcal)[1]	**Meal size (kcal)[2]**
Total mass (kg)	**.314***	.096
Fat mass (kg)	**-.259***	-.157
Fat-free mass (kg)	**.442*****	**.245***
Body fat (%)	**-.374****	-.192
BMI ($kg \bullet m^{-2}$)	.054	-.073
RMR ($kcal \bullet day^{-1}$)	**.311****	.089
TDEE ($kcal \bullet day^{-1}$)	**.469*****	**.301***

[1]Controlling for study; [2]Controlling for study and sex. *p<.05; **p<.01; ***p<.001.

6.3.5 The strongest predictor of meal size

When fat mass, fat-free mass, RMR, MVPA, PAEE, TDEE and energy density were entered in a stepwise regression controlling for study (Table 6-6), model 1 included TDEE ($F(2,67)=12.17$, p<.001; R^2 = 26.6%; Figure 6-2), and model 2 also included energy density (ΔR^2=4.2%, p=.049) such that both TDEE and energy density independently predicted meal size and together accounted for 30.8% of the variance in meal size. Age and sex were also entered in a final step but did not influence the reported outcomes and were not included for analysis in these models.

Table 6-6 Regression coefficients showing the effect of total daily energy expenditure (TDEE) and energy density (ED) on meal size using stepwise multiple regression

Model 1				**Model 2**			
	B	**Standard error**	**β**		**B**	**Standard error**	**β**
Constant	461.79	182.89		Constant	-430.27	479.79	
Study	-79.67	59.45	-.14	Study	8.38	72.89	.02
TDEE	.24	.05	.47**	TDEE	.23	.05	.46**
				ED	586.19	292.54	.26*

*p<.05; **p<.001.

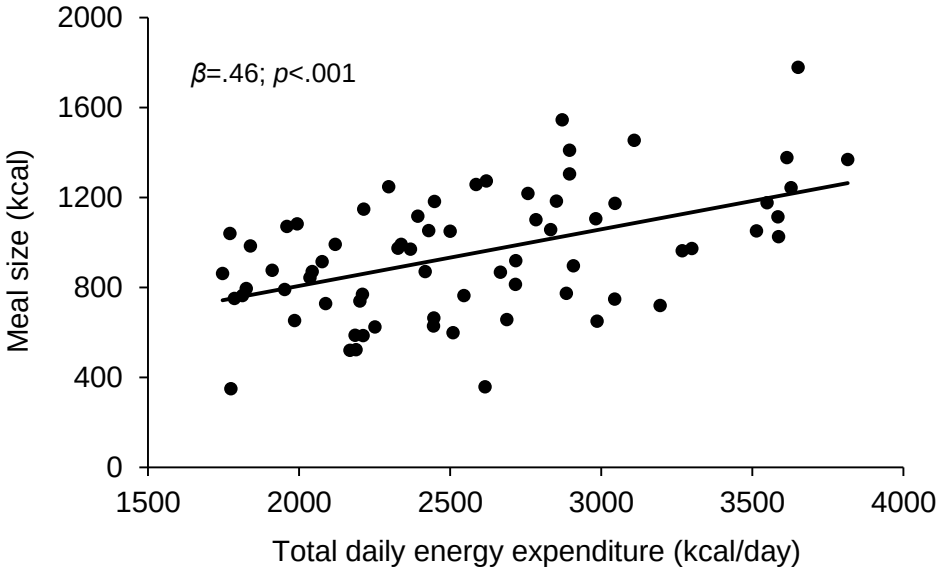

Figure 6-2 Scatter plot and standardized beta coefficient illustrating the relationship between total daily energy expenditure and meal size.[1]

6.3.6 Correlations among the components of physical activity and appetite sensations, SQ, eating behaviour traits, food reward and appetite-related peptides

After controlling for study, none of the components of physical activity were associated with fasting ratings of hunger, fullness, desire to eat or PFC, nor with morning hunger AUC (over 3h). Morning fullness AUC was negatively associated with PAL ($r(67)= -.30$, $p=.01$), PAEE ($r(67)= -.35$, $p=.003$), vigorous PA ($r(67)= -.32$, $p=.007$), MVPA ($r(67)= -.26$, $p=.03$) and total PA ($r(67)= -.25$, $p=.04$). Morning desire to eat AUC was positively associated with VO_{2max} ($r(67)= .25$, $p=.04$), PAL ($r(67)= .24$, $p=.048$), moderate PA ($r(67)= .27$, $p=.03$), MVPA ($r(67)= .27$, $p=.03$) and morning PFC AUC was positively associated with VO_{2max} ($r(67)= .26$, $p=.04$), PAL ($r(67)= .29$, $p=.01$), PAEE ($r(67)= .28$, $p=.02$), moderate PA ($r(67)= .25$, $p=.04$), vigorous PA ($r(67)= .27$, $p=.03$), MVPA ($r(67)= .29$, $p=.02$) and total PA ($r(67)= .27$, $p=.02$). The satiety quotient was only negatively associated with PAEE ($r(67)= -.25$, $p=.04$).

As shown in Table 6-7, none of the components of physical activity or body composition were correlated with eating behaviour traits related to binge eating, restraint, disinhibition, craving control or food reward (liking or wanting for high-fat

[1] Scatter plots illustrating the relationship between PAEE and meal size, and RMR and meal size can be found in Appendix B.

foods) except for TDEE which was negatively associated with binge eating score, but this did not remain significant when controlling for sex.

Table 6-7 Associations between components of body composition, energy expenditure, physical activity, eating behaviour traits and food reward

	Restraint	**Disinhibition**	**BES**	**Craving control**	**Liking**	**Wanting**
Total mass (kg)	-.113	-.056	-.134	-.021	-.102	-.042
BMI ($kg \bullet m^{-2}$)	.104	-.002	-.025	.000	-.091	-.071
Fat mass (kg)	.137	.096	.119	.136	-.084	-.133
Fat-free mass (kg)	-.181	-.103	-.192	-.087	-.058	.025
Body fat (%)	.195	.130	.198	.118	-.018	-.089
TDEE ($kcal \bullet day^{-1}$)	-.179	-.140	**-.235***	-.052	.017	.136
PAEE ($kcal \bullet day^{-1}$)	-.123	-.033	-.162	-.116	.050	.105
PAL	-.123	-.033	-.162	-.116	.050	.105
VO_{2max} ($mL \bullet kg^{-1} \bullet min^{-1}$)[1]	-.006	-.130	-.212	.030	-.101	-.013
Light PA ($min \bullet day^{-1}$)	-.076	-.085	-.155	-.017	.091	.111
Moderate PA ($min \bullet day^{-1}$)	-.088	-.138	-.195	-.040	.144	.215
Vigorous PA ($min \bullet day^{-1}$)	-.044	-.119	-.144	-.005	.030	.130
Total PA ($min \bullet day^{-1}$)	-.088	-.126	-.196	-.025	.113	.170
MVPA ($min \bullet day^{-1}$)	-.079	-.147	-.197	-.029	.111	.204

[1]n=69. *p<.05.

The associations among the components of physical activity, body composition, energy expenditure, meal size and fasting appetite-related peptides including insulin (and HOMA), leptin and acylated ghrelin in a subsample of 34 participants are presented in Table 6-8. After controlling for percentage body fat, none of the components of physical activity were associated with any of the fasting peptides of appetite, indicating that fat mass was the key variable related to appetite-related peptides.

Table 6-8 Associations between body composition, energy expenditure, physical activity, meal size and fasting appetite-related peptides (*n*=34)

	Insulin ($mU \bullet L^{-1}$)[1]	**HOMA[1]**	**Leptin ($pg \bullet mL^{-1}$)[1]**	**Ghrelin ($pg \bullet mL^{-1}$)[2]**
Total mass (kg)	.063	.106	-.201	-.139
BMI ($kg \bullet m^{-2}$)	**.401***	**.420***	.189	-.065
Fat mass (kg)	**.442****	**.402***	**.624*****	.240
Fat-free mass (kg)	-.157	-.091	**-.531****	-.241
Body fat (%)	**.425***	**.361***	**.782*****	.348
TDEE ($kcal \bullet day^{-1}$)	-.248	-.193	**-.549****	-.256
PAEE ($kcal \bullet day^{-1}$)	-.288	-.247	**-.408***	-.178
PAL	-.285	-.279	-.283	-.151
VO_{2max} ($mL \bullet kg^{-1} \bullet min^{-1}$)	-.304	-.288	**-.448****	-.124
Light PA ($min \bullet day^{-1}$)	-.300	-.302	**-.392***	**-.503***
Moderate PA ($min \bullet day^{-1}$)	-.252	-.252	-.232	-.204
Vigorous PA ($min \bullet day^{-1}$)	**-.397***	**-.367***	**-.434***	-.121
Total PA ($min \bullet day^{-1}$)	**-.365***	**-.358***	**-.426***	-.395
MVPA ($min \bullet day^{-1}$)	**-.347***	-.332	**-.352***	-.181
Meal size (kcal)	-.008	.018	-.120	-.017

[1]*n*=34; [2]*n*=21. *p<.05; **p<.01; ***p<.001.

6.3.7 Physical activity level analysis

To address the inter-relationships among physical activity level, body composition and meal size, sex-stratified tertiles of daily minutes of MVPA were created (LoMVPA, ModMVPA and HiMVPA). The groups differed significantly in terms of daily minutes of MVPA, BMI, adiposity, TDEE, PAL and daily steps (Table 6-9).

To further explore the impact of physical activity in the relationship between body composition (fat mass and fat-free mass) and meal size, correlations were conducted within each MVPA group. As shown in Figure 6-3, after controlling for study, the only significant association between fat mass and meal size was in those with the highest levels of MVPA (HiMVPA), whereas the association between fat-free mass and meal size was present in all groups, albeit not statistically significant in ModMVPA. However, the association between fat mass and meal size in HiMVPA did not remain significant when also controlling for fat-free mass ($r(19)= -.23$, $p=.32$).

Table 6-9 Characteristics of MVPA groups

	LoMVPA	**ModMVPA**	**HiMVPA**	***P*-value**
N (% female)	23 (61)	24 (63)	23 (61)	
MVPA (min•day^{-1})	80.2 ± 16.0	125.4 ± 20.7	203.4 ± 43.0	**<.001**
Age (years)	31.0 ± 10.4	28.5 ± 6.9	29.0 ± 9.7	.62
BMI (kg•m^{-2})	23.6 ± 2.6	22.7 ± 2.1	21.7 ± 1.7	**.02**
Total mass (kg)	68.4 ± 13.2	64.0 ± 9.6	64.6 ± 9.3	.33
Fat mass (kg)	18.4 ± 4.9	14.7 ± 5.0	13.4 ± 5.1	**.003**
Fat-free mass (kg)	50.0 ± 11.9	49.3 ± 10.3	51.2 ± 10.8	.83
Body fat (%)	27.2 ± 6.8	23.2 ± 7.9	21.2 ± 1.8	**.03**
RMR (kcal•day^{-1})	1543.8 ± 284.0	1663.8 ± 278.1	1677.2 ± 226.5	.18
TDEE (kcal•day^{-1})	2218 ± 443	2382 ± 485	2455 ± 408	**.001**
PAL	1.50 ± 0.10	1.64 ± 0.12	1.91 ± 0.19	**<.001**
Daily steps	7362.0 ± 2016.2	10364.2 ± 2697.3	12512.5 ± 3207.2	**<.001**
Meal size (kcal)	896.8 ± 267.5	921.9 ± 244.0	1035.4 ± 315.4	.20

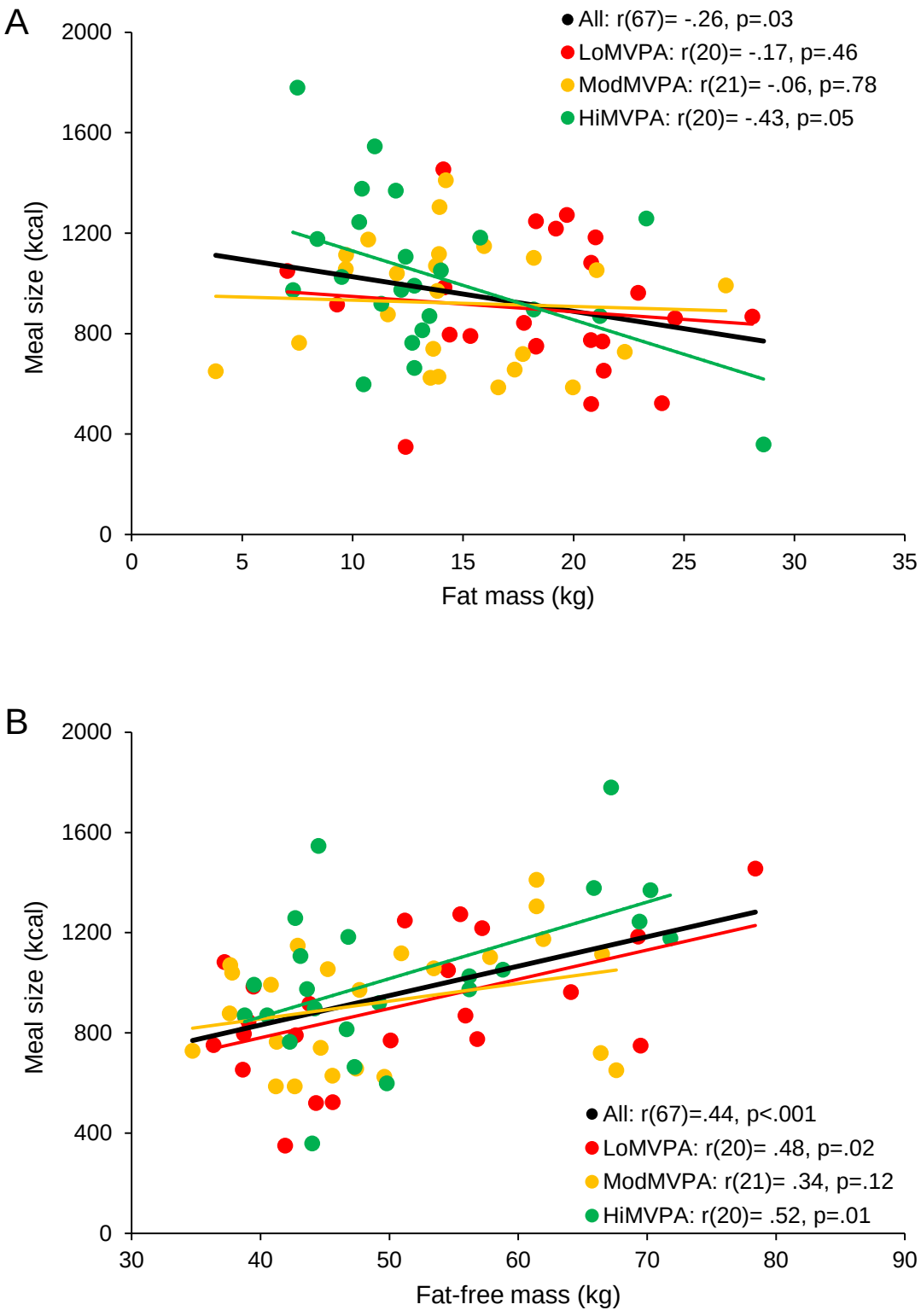

Figure 6-3 Relationship between body composition (fat mass, A; fat-free mass, B) and meal size within groups of moderate-to-vigorous physical activity.

6.4 Discussion

This study examined relationships among the components of physical activity, food intake and appetite control in relatively active non-obese individuals. It was imperative to include measures of body composition and energy expenditure due to their inter-relationships with physical activity. Importantly, all the variables were objectively-assessed, and physical activity and TDEE were habitual and measured in free-living conditions. The results showed clear negative associations between physical activity and adiposity, and positive associations with TDEE. Individually, body composition (both fat mass and fat-free mass), RMR, TDEE, and the components of physical activity (except for light physical activity) were associated with food intake. However, multiple regression analyses revealed that TDEE was the strongest predictor of food intake, followed by dietary energy density.

6.4.1 Physical activity and total daily energy expenditure as drivers of food intake

Physical activity (daily minutes) was associated with all components of energy expenditure, including RMR, PAEE and TDEE. Several positive relationships between various components of physical activity, energy intake and motivation to eat were found, suggestive of a drive to eat originating from physical activity, and a coupling between energy expenditure and energy intake. As discussed in the previous chapter, these data fit within the right-hand side of the J-shape relationship observed by Mayer et al. (1956), where energy intake increases with physical activity level in individuals of similar body weight. This was also apparent when the participants were divided into groups of daily minutes of MVPA.

However, this study suggests that the associations between physical activity and energy intake could be mediated by the influence of physical activity on TDEE, with habitual free-living TDEE being the strongest predictor of energy intake among the components of physical activity and energy expenditure in this non-obese population. This was also found with TDEE measured in a respiratory chamber (Piaggi et al., 2015), but is in contrast to evidence demonstrating that RMR was a stronger determinant of energy intake than TDEE (Hopkins, Finlayson, et al., 2016). However, contrary to previous research that was conducted in overweight and obese individuals within laboratory settings and may have artificially curtailed physical activity (Hopkins, Finlayson, et al., 2016; Piaggi et al., 2015), the current study was conducted in non-obese relatively active individuals and provides a different perspective as it examines the associations among objectively-measured free-living habitual TDEE, physical

activity and food intake. It can be argued that daily energy intake in the present study was measured in conditions that restricted physical activity in habitually active individuals and may not represent usual intake, but previous evidence suggests that intake is not down-regulated with acute reductions in physical activity (Stubbs, Hughes, Johnstone, Horgan, et al., 2004). This is also supported by the significant positive associations observed between physical activity and energy intake in the current study, and also when measured in free-living conditions (Tucker, 2016). Alongside TDEE, dietary energy density was also an independent predictor of energy intake, corroborating previous evidence (Hopkins, Finlayson, et al., 2016). In line with the previous chapters of this thesis, the importance of favouring a lower energy-dense diet to avoid an overconsumption of energy and positive energy balance is very important for the maintenance of a healthy body weight (Rolls, 2000).

6.4.2 Towards understanding the inter-relationships among physical activity, body composition, energy intake and appetite control in non-obese individuals

In addition to physical activity and energy expenditure being correlated with energy intake, in these non-obese participants, significant associations were found between fat-free mass and energy intake (positive) and fat mass and energy intake (negative). This applied for both meal size and daily energy intake. Therefore, energy intake and the motivation to eat are not only driven by metabolic requirements derived from fat-free mass, a strong determinant of RMR, as previously shown (Blundell, Finlayson, et al., 2015), but this study suggests that energy intake is also driven by dispensable energy expenditure stemming from physical activity. However, together comprising the majority of the elements of daily energy requirements, it is not surprising that TDEE was the strongest predictor of food intake.

As well as the positive association between fat-free mass and energy intake, a negative association between fat mass and energy intake was also revealed, supporting previous evidence in lean individuals (Blundell, Finlayson, et al., 2015). This is also in line with the negative association between fat mass and hunger found in lean individuals (Cugini et al., 1998). Interestingly, as demonstrated by the MVPA group analyses, it appears that this inhibitory effect of fat mass could be strongest in those with the highest levels of MVPA (and lowest levels of body fat). MVPA was also negatively associated with insulin and HOMA, but likely via an effect on adiposity as the correlations became non-significant when controlling for body fat. Nevertheless, in non-obese highly active individuals, it seems very plausible that the negative effect of fat mass on energy intake is mediated by increased insulin sensitivity. However, given

the small sample size of the MVPA groups and exploratory nature of the analyses, more research is needed to confirm these findings and elucidate underlying mechanisms.

It could be proposed that physical activity enhances the sensitivity of the appetite control system through improvements in body composition and in turn insulin sensitivity, leading to a stronger homeostatic satiety response to food (Flint et al., 2007; Morton et al., 2006; Schwartz et al., 2000). This is plausible and meaningful as an indirect rather than a direct effect of physical activity. In the few studies that have examined physical activity, insulin sensitivity and appetite control in overweight and obese individuals, those that demonstrated improvements in appetite control with 12 weeks of exercise training coincided with improvements in both insulin sensitivity and body fat (Guelfi et al., 2013; Martins et al., 2010; Martins et al., 2013), but also independent of significant body fat loss (Sim et al., 2015). Therefore, whether physical activity enhances appetite control in individuals with obesity independent of body fat loss remains unclear. This will be further addressed in the following chapter.

6.4.3 Limitations

It is important to acknowledge that in this study, both physical activity and TDEE were measured with the same device rather than with two independent measures (e.g. accelerometry for physical activity and doubly-labelled water for TDEE). Nevertheless, the SWA has been validated and has shown good accuracy in predicting TDEE (Johannsen et al., 2010; St-Onge et al., 2007). Furthermore, PAEE was derived from TDEE, but was strongly correlated to minutes of measured total physical activity and MVPA, supporting the validity of its use. Another limitation to the SWA is that it cannot differentiate between structured exercise and non-exercise physical activity; therefore, specific conclusions regarding exercise cannot be derived from these data. These data, however, highlight the importance of incorporating MVPA into daily life, regardless of type or structure. Finally, as correlation is not proof of causality and does not permit causal inference, most of the discussion points remain theoretical and await confirmation in future studies. Indeed, replication is a key feature of strong science.

6.4.4 Conclusions

This study demonstrated that physical activity was positively associated with daily energy expenditure and negatively associated with adiposity. Further, fat-free mass, physical activity, and TDEE were all associated with meal size, suggesting these could be drivers of energy intake. However, the strongest predictor of energy intake was

TDEE, followed by dietary energy density. Furthermore, in these non-obese individuals, fat mass was significantly negatively correlated with meal size. This inhibitory effect of fat mass on food intake could be strongest in those with the highest levels of physical activity, which may be linked to the lower fat mass and greater insulin sensitivity observed in these individuals. These results support the theory that higher levels of physical activity enhance the sensitivity of appetite control, with individuals being able to match energy intake to energy expenditure.

Chapter summary:

- Habitual physical activity was positively associated with energy expenditure and negatively associated with adiposity.
- Physical activity was significantly and positively associated with energy intake, but total daily energy expenditure was the strongest predictor of meal size.
- In non-obese individuals, fat-free mass was positively associated with energy intake, whereas fat mass was negatively associated with energy intake, consistent with the proposition that fat-free mass drives energy intake and fat mass inhibits it.
- The effect of fat mass on energy intake could be moderated by physical activity, adiposity or insulin sensitivity.

Chapter 7 – Impact of a 12-week exercise intervention on homeostatic and hedonic appetite control in inactive overweight and obese individuals (DIVERSE – DrIVERS of Eating behaviour during chronic energy expenditure)

Chapter aims:

- Assess the impact of a 12-week exercise intervention on homeostatic and hedonic processes of appetite control in response to foods varying in fat content in inactive overweight and obese individuals.
- Examine the influence of 12 weeks of exercise training on associations among determinants of energy intake in response to foods varying in fat content.

7.1 Introduction

As proposed in Chapter 2, in overweight and obese individuals, exercise training may exert a dual-process action on appetite control by increasing fasting hunger and the drive to eat, but also by enhancing post-meal satiety (King et al., 2009). Physiological adaptations occurring with habitual physical activity and exercise training appear to improve the sensitivity of appetite control, at least in the case of satiety (Guelfi et al., 2013; Long et al., 2002; Martins et al., 2010; Martins et al., 2013; Martins, Truby, et al., 2007; Van Walleghen et al., 2007). Very little evidence in the literature exists regarding the impact of physical activity on satiation (which reflects the control over meal size). In Chapter 4, there was no effect of physical activity level on satiation or passive overconsumption in non-obese individuals (Beaulieu, Hopkins, et al., 2017a). This study showed that manipulating the fat content and energy density of a lunch meal increased meal size regardless of physical activity level. As such, high energy density foods may overpower any influence of physical activity on mechanisms underpinning meal size. However, in overweight and obese individuals, a reduction in meal size at a high-fat meal after exercise training was found by Caudwell, Finlayson, et al. (2013), but whether this is a result of improvements in homeostatic or hedonic appetite control (or both) is unknown.

Chronic hyperinsulinemia seen with obesity has been proposed as a potential factor involved in disrupted homeostatic appetite control (i.e. satiety signalling) and passive overconsumption (Flint et al., 2007; Speechly & Buffenstein, 2000). Moreover, it has been proposed that insulin sensitivity mediates the strength of appetite-related peptides such as GLP-1 and CCK (Morton et al., 2006; Schwartz et al., 2000), which are involved in the processes of satiation and satiety (de Graaf et al., 2004; Gibbons et al., 2013; Gibbons et al., 2016). Several appetite-related peptides, namely ghrelin, PYY and GLP-1, have also been found to be impacted by acute and chronic exercise (Stensel, 2010; Thackray et al., 2016). Improvements in insulin sensitivity (Borghouts & Keizer, 2000) and/or body composition (Shaw et al., 2006; Stiegler & Cunliffe, 2006) that accompany exercise training, as well as changes in the secretion of the aforementioned appetite-related peptides, may therefore contribute to an enhancement in homeostatic appetite control in overweight and obese individuals.

Food intake is not only influenced by homeostatic signals. Importantly, food hedonics can override weak physiological signals and lead to overconsumption (Blundell & Finlayson, 2004; Erlanson-Albertsson, 2005). These influences may be more prominent in individuals with overweight and obesity (Horner et al., 2016; Nijs et al., 2010), and are proposed factors contributing to passive overconsumption (Blundell & MacDiarmid, 1997). Food hedonics are also potentially influenced by physical activity, but evidence has been inconsistent. One study found that an acute bout of either resistance or aerobic exercise reduced the hedonic preference for high-fat foods in healthy weight individuals (McNeil, Cadieux, Finlayson, Blundell, & Doucet, 2015), whereas another study found no impact of acute bouts of continuous or intermittent exercise in overweight/obese individuals (Martins et al., 2015). However, in overweight and obese individuals, a heightened hedonic response to food after acute exercise was only present in individuals who showed a smaller exercise-induced reduction in fat mass during a 12-week exercise intervention (Finlayson, Caudwell, et al., 2011). This response to acute exercise was independent of exercise training and weight loss. Furthermore, a lower rewarding value of foods (liking and wanting) has been observed in lean active compared to overweight inactive males (Horner et al., 2016), while 12 weeks of exercise training did not lead to any changes in the rewarding value of food in obese individuals (Martins et al., 2017). While the exercise intervention in these obese individuals induced significant reductions in body weight (-1.2kg; ~1.2%), perhaps a larger and more clinically significant weight loss is required to impact on food hedonics. These results suggest that firstly, physical activity may influence food hedonics differently according to an individual's body weight status, and secondly, that in overweight and obese individuals undergoing exercise training, the impact on food

hedonics may also depend upon the degree of weight loss or change in body composition.

7.1.1 Objective & hypotheses

The objective of this study was to investigate whether satiation, satiety and the hedonic liking and wanting for high-fat foods are improved on exposure to high-fat (HFAT) and high-carbohydrate (HCHO) foods during a 12-week exercise intervention in inactive overweight and obese individuals. The study also examined whether exercise training mitigates passive overconsumption of dietary fat. The study also aimed to explore the determinants (correlates) of appetite control associated with HFAT and HCHO intake, such as body composition, fasted appetite-related peptides and food hedonics, and any changes in these associations observed with exercise training. Based on the aforementioned literature and on the previous chapters of this thesis, it was hypothesised that post-meal satiety, but not satiation or passive overconsumption, would improve with exercise training.

7.2 Methods

7.2.1 Participants

Sixty-four overweight and obese men and women aged 18-55 years were recruited (46 participants completed the study (30 females and 16 males) and fasting blood samples were taken in a subsample of 32 participants). Participants were screened on the following inclusion criteria: BMI between 26.0-38.0 kg/m^2, non-smoker, inactive (≤ 2h per week of exercise over the previous 6 months), weight stable (±2 kg for previous 3 months), not currently dieting or participating in a weight loss regime, no history of eating disorders, not taking any medication known to affect metabolism or appetite, and acceptance of the study foods. Participants were asked to keep lifestyle habits and activities constant throughout the study. The study was approved by the Leeds West NHS Research Ethics Committee (09/H1307/7). Participants provided written informed consent prior to taking part.

7.2.2 Study design

Data from a previously conducted study within the Human Appetite Research Unit at the University of Leeds (UK) archived under Good Clinical Practice guidelines for data security and preservation were used for these secondary analyses. Participants completed a 12-week exercise intervention in which they exercised 5 days per week under supervision of research staff in the Human Appetite Research Unit. At baseline (week 0) and post-intervention (week 13), participants completed a measures test day to assess a range of physiological and eating behaviour variables (Figure 7-1; further described below). Daily food intake was also measured at baseline and post-intervention on two separate test meal days. These days were separated by at least one day and in a randomised crossover order. The measures and meal days were also completed at week 6 but not reported in this chapter as this thesis aims to compare individuals in the inactive and active states. The ingredients of the foods provided during the meal days were covertly manipulated to be HFAT (37.7% carbohydrate, 54.4% fat, 7.9% protein; energy density: 2.49 ± 0.27 kcal/g) or HCHO (72.4% carbohydrate, 19.3% fat, 8.3% protein; energy density: 1.58 ± 0.20 kcal/g; see Section 7.2.4). Prior to each test day, participants fasted overnight (10-12 hours) and refrained from consuming alcohol for 24 hours.

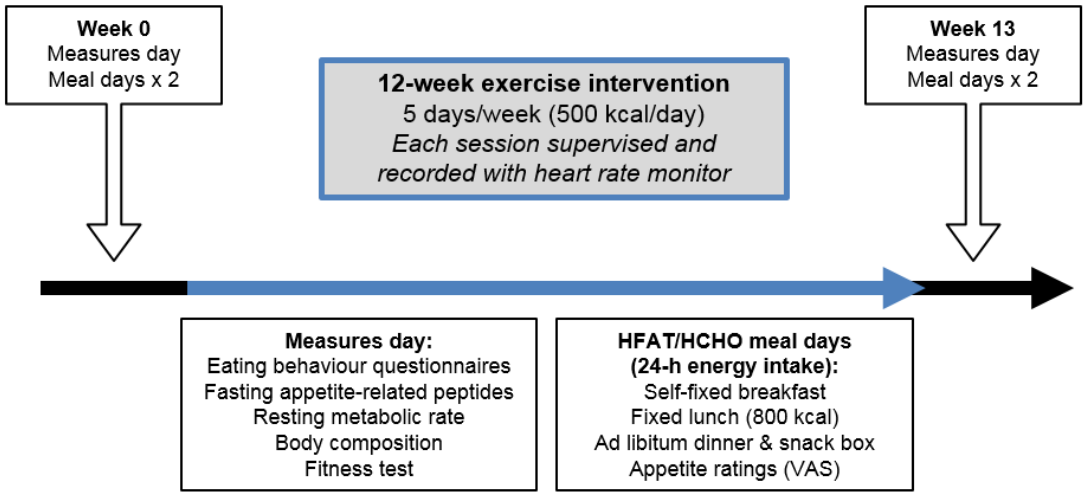

Figure 7-1 Experimental protocol.

7.2.3 Measures days

In the week before (week 0) and after (week 13) the exercise intervention, body composition (fat mass and fat-free mass), RMR, VO_{2max} and eating behaviour traits (TFEQ and BES) were measured as previously described in Chapter 3.

7.2.3.1 Appetite-related peptides

A fasting blood sample was taken by venepuncture in a subsample of 32 participants for the measurement of leptin, total ghrelin, insulin, glucose, active GLP-1 and total PYY. Blood was drawn in EDTA vacutainers containing aprotinin (50 µL/mL blood), dipeptidyl peptidase IV inhibitor (10 µL/mL blood), and Pefabloc SC (50 µL/mL blood) for preservation of the peptides, and centrifuged for 10 minutes at 4ºC at 4000 rpm. Plasma obtained was aliquoted and stored at -70ºC until analysis at the Gastroenterology and Hepatology Unit, Medical Sciences, Uppsala University, Uppsala, Sweden. Prior to analysis, plasma was thawed and additional protease inhibitors were added (0.5 µM of Sigmafast (1x) and dipeptidyl peptidase IV inhibitor). Glucose was analysed by the Department of Clinical Chemistry at the Uppsala Academic Hospital, Uppsala, Sweden. Total ghrelin was measured with an ELISA kit (Millipore, USA). Leptin, insulin, active GLP-1, and total PYY were measured with a fluorescent multiplex ELISA using different coloured magnetic beads (Millipore, USA) and a microtiter plate-based bead counter (Magpix, Luminex, USA). The coefficients of variation for intra-assay precision for leptin, insulin, active GLP-1, and total PYY is 8.3%, and for total ghrelin is 3.4%.

7.2.4 Meal days

7.2.4.1 Self-determined fixed breakfast

Breakfast during the HFAT and HCHO meal days at baseline was ad libitum with cereal, milk, toasted bread, scrambled eggs, and margarine/butter similar in appearance but varying in fat and CHO content (according to the meal day) served in excess of expected consumption (Table 7-1). Water, coffee, tea, and sugar were also offered. At baseline, the participants were free to self-determine the size of their own breakfasts, and were instructed to eat as much or as little as they liked until they reach a comfortable level of fullness. The quantities consumed in HFAT and HCHO at baseline were subsequently replicated for the HFAT and HCHO breakfasts post-intervention to make the energy content of the meal individually fixed. At each eating occasion, food items were weighed before and after consumption to the nearest 0.1 g

and energy intake was subsequently calculated using energy equivalents for protein, fat and carbohydrate of 4, 9 and 3.75 kcal/g, respectively, from the manufacturers' food labels. Upon consumption of breakfast, participants were instructed not to eat or drink any food until their next meal session except from the bottle of water provided.

Table 7-1 Food items and macronutrient composition of the ad libitum HFAT and HCHO breakfast at baseline

	kcal/g	**% CHO**	**% fat**	**% protein**
HFAT	**2.59[1]**	**25.3**	**56.7**	**18.0**
Cornflakes	3.50	89.9	2.1	8.0
Whole milk	0.63	27.9	51.2	20.9
Medium toast	2.66	80.6	5.4	14.0
Eggs	4.38	0.0	76.7	23.3
Margarine	6.31	0.1	99.9	0.0
Sugar	3.75	100.0	0.0	0.0
HCHO	**1.52**	**42.4**	**35.7**	**21.9**
Cornflakes	3.50	89.9	2.1	8.0
Semi skim milk	0.48	39.3	32.1	28.5
Thick toast	2.66	80.6	5.4	14.0
Eggs	1.60	0.0	65.4	34.6
Flora light	3.42	0.0	99.9	0.1
Sugar	3.75	100.0	0.0	0.0

[1]HFAT and HCHO mean values based on ad libitum consumption.

7.2.4.2 Fixed-energy lunch

Four hours after breakfast, the participants returned to the laboratory for lunch. The fixed-energy lunch meal was composed of HFAT or HCHO food items providing 800 kcal on both meal days. The HFAT meal was composed of a cheese sandwich (70 g white bread, 6 g butter, 40 g cheese slices and 20 g iceberg lettuce), crisps, caramel short cake and water (see Table 7-2 for more details). The HCHO meal was composed of a cheese sandwich (90 g bread, 6 g extra light margarine, 20 g low-fat cheese, 20 g iceberg lettuce), light crisps, chocolate chip slice and water. In addition to being matched for energy content, the meals were similar in appearance and weight. Participants had 30 minutes to consume the meal in its entirety, and food items were weighed before and after consumption to the nearest 0.1 g to ensure compliance.

Table 7-2 Food items and macronutrient composition of the fixed energy HFAT and HCHO lunches

	g	kcal	kcal/g	% CHO	% fat	% protein
HFAT	**491.0**	**819.0**	**1.67**	**34.0**	**53.9**	**11.9**
Sandwich	136.0	492.1	3.62	32.1	50.0	17.5
Crisps	20.0	104.8	5.24	35.1	61.8	3.1
Short cake	45.0	222.1	4.94	37.5	58.7	3.7
Water	290.0	0.0	0.00	0.0	0.0	0.0
HCHO	**506.0**	**794.6**	**1.57**	**60.2**	**27.1**	**12.7**
Sandwich	139.0	358.2	2.58	21.5	21.0	57.5
Crisps	40.0	185.4	4.64	48.5	3.7	47.7
Short cake	80.0	251.0	3.14	19.2	7.5	73.3
Water	250.0	0.0	0.00	0.0	0.0	0.0

7.2.4.3 Ad libitum dinner

Four hours after lunch, the participants returned to the laboratory for an ad libitum dinner consisting of a main course, side dish and dessert. The participants were instructed to eat as much or as little as they liked until they reach a comfortable level of fullness. Again, foods were designed to be similar and were presented in the same fashion (see Table 7-3 for details). Food items were weighed before and after consumption to the nearest 0.1 g to determine quantities consumed, and energy intake calculated as previously described.

Table 7-3 Food items and macronutrient composition of the ad libitum HFAT and HCHO dinner meals

	kcal/g	% CHO	% fat	% protein
HFAT	**2.76[1]**	**29.8**	**57.6**	**12.7**
Pizza	2.86	28.6	49.4	22.1
Garlic bread	4.23	34.8	57.2	8.0
Coleslaw	1.43	17.8	78.7	3.6
Snack cakes	4.91	41.7	54.1	4.2
Shortbread	5.14	42.2	53.4	4.4
Crisps	5.16	35.6	59.3	5.0
HCHO	**1.14**	**66.4**	**19.8**	**13.6**
Pizza	2.18	59.4	24.8	15.8
Bread & Flora	2.79	67.5	20.0	12.5
Lettuce	0.13	56.4	21.4	22.2
Tomato	0.17	67.9	15.8	16.4
Cucumber	0.09	60.3	9.7	30.0
Malt loaf	2.93	84.2	6.1	9.7
Swiss rolls	2.74	84.6	10.2	5.3
Apples	0.47	94.7	1.9	3.4

[1]HFAT and HCHO mean values based on ad libitum consumption.

7.2.4.4 Ad libitum snack box

Upon consumption of the dinner, participants were given a snack box containing a selection of pre-weighed HFAT or HCHO foods to eat at home (see Table 7-4). Participants were instructed to eat only from this snack box until they went to bed that evening and to return all elements of the snack box, including empty packaging or partially-eaten foods, the following morning.

Table 7-4 Food items and macronutrient composition of the ad libitum HFAT and HCHO snack boxes

	kcal/g	% CHO	% fat	% protein
HFAT	**4.90[1]**	**40.1**	**53.2**	**6.7**
Crackers	4.97	43.5	50.3	6.3
Cookies	5.09	41.5	53.6	5.0
Flapjacks	4.32	47.3	47.5	5.3
Chocolate	4.78	43.7	49.5	6.7
Peanuts	5.99	5.4	77.4	17.1
HCHO	**2.31**	**84.5**	**9.5**	**5.8**
Jaffa cakes	3.62	76.4	19.1	4.4
Biscuits	3.73	67.5	26.3	6.1
Jelly babies	3.11	92.9	0.3	6.8
Bananas	0.95	92.1	2.9	5.1

[1]HFAT and HCHO mean values based on ad libitum consumption.

7.2.4.5 Passive overconsumption

Passive overconsumption was measured at the ad libitum dinner meal only as it was consumed under controlled laboratory conditions where intake could be accurately quantified. This procedure represented a more valid response compared to the snack box, which was consumed under free-living conditions where intake could not be objectively verified and consumed as one meal. Passive overconsumption was calculated in absolute amounts and also accounting for metabolic adaptations occurring from the exercise intervention and was expressed 3 ways in the current chapter as TDEE was not objectively measured: 1) absolute difference between HFAT and HCHO meal size in grams (PO_g); 2) absolute difference between HFAT and HCHO meal size in kcal (PO_{kcal}); and 3) difference between HFAT and HCHO meal size in kcal accounting for RMR (PO_{RMR}).

7.2.4.6 Appetite ratings and satiety quotient

Appetite ratings were assessed before and after each meal, and at hourly intervals throughout the meal day via VAS for hunger, fullness, desire to eat and PFC using the Electronic Appetite Rating System (Gibbons et al., 2011), as described in Chapter 3. Only the hunger ratings were available for these secondary analyses. AUC was calculated using the trapezoid rule. The SQ (Green et al., 1997), as marker of post-meal satiety was calculated as described in Chapter 3. SQ was calculated after the breakfast and lunch test meals only as food intake was controlled afterwards (no food until the following meal) whereas participants were free to consume from the evening snack box immediately upon leaving the laboratory following the dinner test meal, which may have affected the SQ scores.

7.2.4.7 Food reward

The Leeds Food Preference Questionnaire (LFPQ) was administered during the HFAT and HCHO meal days pre- and post-lunch consumption to determine scores of implicit wanting and explicit liking fat appeal bias to determine preference for high-fat relative to low-fat foods (Finlayson et al., 2008), as described in Chapter 3.

7.2.5 12-week exercise intervention

During the 12-week exercise intervention (5 days per week), each exercise session was individually tailored to expend 500 kcal at an intensity of 70% of age-predicted heart rate maximum (HR_{max}) and to ensure compliance to the exercise intensity and duration, participants wore a heart rate monitor (Polar RS400, Polar, Finland) during each session. A selection of aerobic exercise equipment was available (i.e. treadmill, rower, cycle ergometer, and elliptical) from which the participants were free to choose and change within each session as long as they met the energy expenditure requirements. Calibration of the exercise duration to expend 500 kcal at 70% HR_{max} was based on the relationship between heart rate, VO_2, and VCO_2 during a maximal aerobic capacity test, along with standard stoichiometric equations (Peronnet & Massicotte, 1991), allowing for the calculation of energy expenditure (kcal per minute, using energy equivalents of 3.75 kcal/g and 9 kcal/g for carbohydrate and fat, respectively) at 70% HR_{max} and duration of time needed to expend 500 kcal. This was also performed at week 6 of the intervention to account for changes in energy metabolism.

7.2.6 Statistical analysis

Paired sample *t*-tests were used to determine differences in participant characteristics and passive overconsumption pre- and post-intervention. Differences in ad libitum energy intake and SQ at each meal were examined with two-way ANOVAs, with the within-subject factors of meal condition (HFAT, HCHO) and exercise training (baseline, post-intervention). Differences in appetite sensations, post-prandial SQ and food reward (liking and wanting) were identified with three-way ANOVAs, with the within-subject factors of meal condition (HFAT, HCHO), exercise training (baseline, post-intervention) and time/food consumption. To control for the influence of the change in body composition occurring through the exercise intervention on the above variables, ANCOVAs were also performed with the change in percentage body fat added as a covariate. Change scores from pre- to post-training were calculated for the variables and Pearson's correlations were conducted to identify correlates of exercise-induced changes in energy intake under HFAT and HCHO conditions. Partial correlations controlling for sex or percentage body fat (where appropriate) were also conducted.

7.3 Results

7.3.1 Compliance with the intervention

Estimated exercise-induced energy expenditure based on heart rate monitoring during the intervention revealed that participants expended on average 27499 ± 3581 kcal over the 12 weeks, equating to a weekly energy expenditure of 2292 ± 298 kcal. This equates to >91% of the prescribed energy expenditure during the exercise intervention.

7.3.2 Participant characteristics

Participant characteristics at baseline and post-intervention can be found in Table 7-5. The exercise-training intervention led to a significant reduction in total mass, body fat percentage, fat mass, waist circumference, and an increase in fat-free mass and VO_{2max}. For the fasting appetite-related peptides, the exercise intervention led to a reduction in leptin, and an increase in GLP-1 and total PYY. The increase in ghrelin approached significance. There was also a significant reduction in disinhibition and binge eating score after the exercise intervention.

Table 7-5 Participant characteristics at baseline (week 0) and post-intervention (week 13)

	Week 0	Week 13	Change	*P*-value
Age (years)	43.2 ± 7.5	-	-	-
BMI ($kg \bullet m^{-2}$)	30.5 ± 3.8	29.9 ± 4.0	-0.60	**<.001**
Total mass (kg)	87.6 ± 14.3	85.7 ± 14.2	-1.81	**<.001**
Body fat (%)	40.0 ± 7.6	38.1 ± 8.2	-1.94	**<.001**
Fat mass (kg)	35.1 ± 9.2	32.8 ± 9.8	-2.24	**<.001**
Fat-free mass (kg)	52.5 ± 10.4	52.9 ± 10.0	0.44	**.02**
Waist circumference (cm)	101.6 ± 10.6	97.9 ± 10.8	-3.70	**<.001**
RMR ($kcal \bullet 24h^{-1}$)	1694.7 ± 311.9	1733.0 ± 279.1	38.24	.24
VO_{2max} ($mL \bullet kg^{-1} \bullet min^{-1}$)	33.4 ± 8.1	39.1 ± 6.8	5.68	**<.001**
Glucose ($mmol \bullet L^{-1}$)[1]	4.9 ± 0.8	4.7 ± 1.0	-0.22	.37
Total ghrelin ($pg \bullet mL^{-1}$)[1]	544.1 ± 256.9	610.7 ± 291.6	66.55	.06
Leptin ($ng \bullet mL^{-1}$)[1]	40423.9 ± 28522.7	32590.8 ± 28484.2	-7833.04	**.004**
Insulin ($ng \bullet L^{-1}$)[1]	996.0 ± 538.1	928.8 ± 547.8	-67.25	.36
GLP-1 ($ng \bullet L^{-1}$)[2]	31.7 ± 18.1	41.2 ± 30.9	9.55	**.02**
Total PYY ($ng \bullet L^{-1}$)[3]	60.0 ± 38.7	80.6 ± 59.8	20.63	**.048**
Restraint	7.5 ± 3.7	7.1 ± 4.0	-0.39	.45
Disinhibition	8.2 ± 3.4	7.5 ± 3.5	-0.70	**.02**
Susceptibility to hunger	5.1 ± 3.5	4.9 ± 3.6	-0.21	.55
Binge eating score	11.9 ± 7.1	10.4 ± 7.5	-1.53	**.02**

[1]*n*=31; [2]*n*=23; [3]*n*=27.

7.3.3 Fixed energy intake: breakfast and lunch

For energy intake at breakfast, which was self-determined from ad libitum intake at baseline and fixed post-intervention, there was a main effect of condition ($F(1,45)=43.47$, $p<.001$) with intake being greater in the HFAT (790.0 ± 294.7 kcal) compared to HCHO (538.0 ± 163.4 kcal), and a main effect of exercise training ($F(1,45)=20.61$, $p<.001$), with participants consuming 11 kcal less overall post-intervention compared to baseline.[2] There was no interaction between condition and exercise training ($F(1,45)=0.08$, $p=.78$).

[2] As this was a fixed meal, this significant result is unexpected and likely due to the low variability in energy intake at the test meal. This reduction of 11 kcal is small and not meaningful.

For energy intake at lunch (mean of HFAT and HCHO: 794.8 ± 17.0 kcal), by design, there was no effect of condition (F(1,45)=2.91, p=.10), exercise training (F(1,45)=0.67, p=.42), or interaction between condition and exercise training (F(1,45)=0.01, p=.92).

7.3.4 Ad libitum energy intake: dinner and evening snack box

For energy intake at dinner (Figure 7-2), there was a main effect of condition (F(1,45)=223.07, p<.001) with energy intake being greater in HFAT compared to HCHO, and a main effect of exercise training (F(1,45)=7.81, p=.008), with an overall reduction in energy intake of 91 kcal post-intervention. There was no significant interaction between condition and exercise training (F(1,45)=2.59, p=.12).

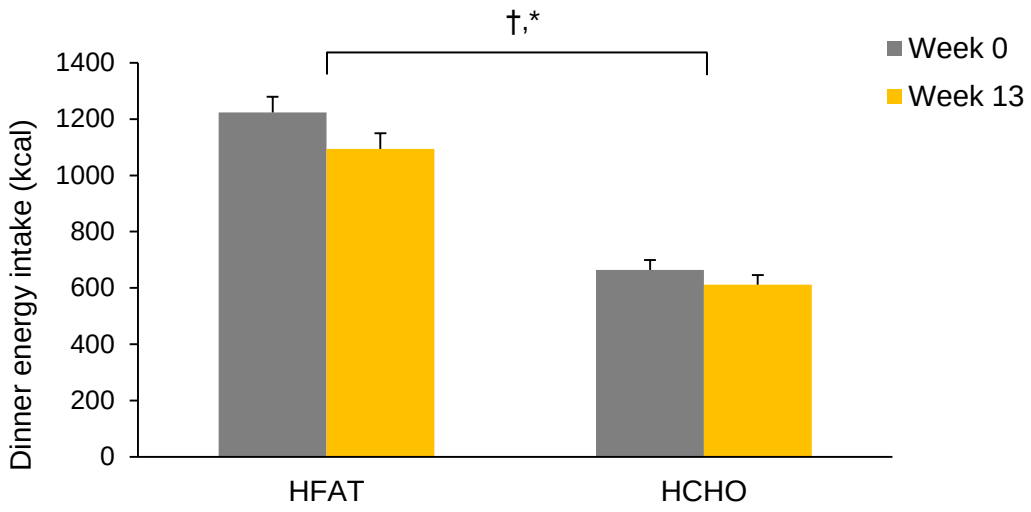

Figure 7-2 Ad libitum energy intake (meal size) at dinner in the HFAT and HCHO conditions at baseline (week 0) and post-intervention (week 13). †Main effect of condition (HFAT vs. HCHO) p<.001. *Main effect of exercise training (week 0 vs. week 13) p=.008.

For energy intake at the evening snack box (Figure 7-3), there was no main effect of condition ($F(1,45)=2.86$, $p=.10$) or exercise training ($F(1,45)=0.08$, $p=.77$), but the interaction between condition and exercise training approached significance ($F(1,45)=3.63$, $p=.06$), with post hoc analyses demonstrating a difference in snack box intake between HFAT and HCHO post-intervention ($p=.02$).

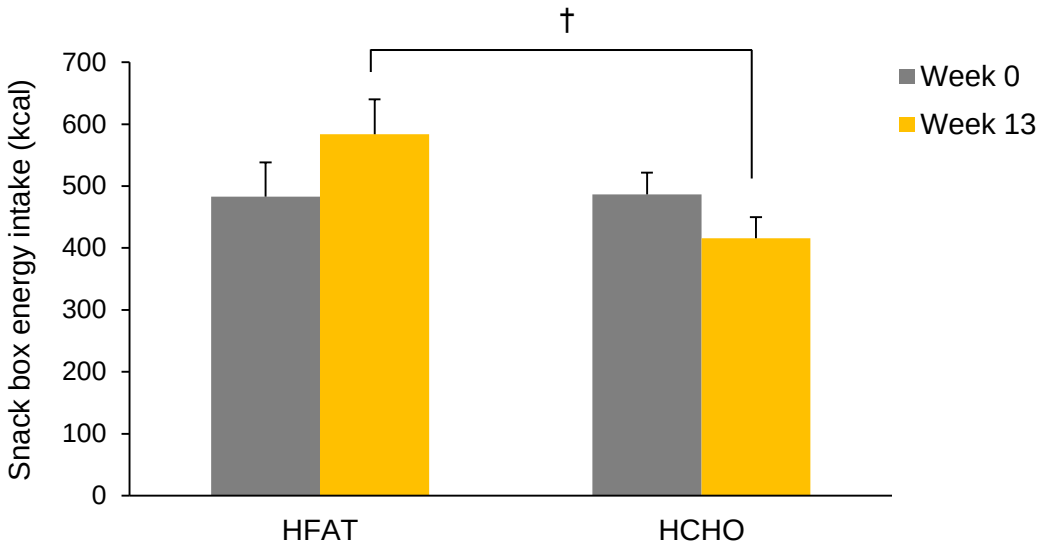

Figure 7-3 Ad libitum energy intake at evening snack box in the HFAT and HCHO conditions at baseline (week 0) and post-intervention (week 13). †HFAT vs. HCHO $p=.02$.

7.3.5 Passive overconsumption

There was no significant difference in passive overconsumption at dinner in grams or kcal at baseline and post-intervention, but the reduction in passive overconsumption after exercise-training when accounting for RMR approached significance (Table 7-6).

Table 7-6 Parameters of passive overconsumption at dinner at baseline (week 0) and post-intervention (week 13)

	Week 0	**Week 13**	***P*-value**
PO_g (g)	-64.2 ± 224.9	-81.0 ± 153.8	.61
PO_{kcal} (kcal)	559.8 ± 318.1	481.8 ± 254.6	.12
PO_{RMR} (%)	33.9 ± 21.2	27.9 ± 13.7	.07

7.3.6 Total daily energy intake

For total daily energy intake (Table 7-7), there was a main effect of condition ($F(1,45)=229.75$, $p<.001$) but not of exercise training ($F(1,45)=1.73$, $p=.20$), and the interaction between condition and exercise training approached significance ($F(1,45)=3.43$, $p=.07$). Post hoc analyses showed that total daily energy intake decreased post-intervention relative to baseline in HCHO, but not HFAT (see Table 7-7).

Table 7-7 Total daily energy intake in HCHO and HFAT at baseline (week 0) and post-intervention (week 13)

	Week 0	**Week 13**	***P*-value**
HCHO (kcal)	2501.4 ± 542.2	2327.0 ± 477.8	.004
HFAT (kcal)	3401.4 ± 763.5	3410.4 ± 799.4	.93

Interim summary 1:

- The exercise intervention:
  - Improved body composition, RMR and VO_{2max};
  - Reduced fasting leptin and increased fasting GLP-1 and PYY, and tended to increase fasting ghrelin;
  - Improved behavioural traits favouring overconsumption (disinhibition and BES);
  - Reduced dinner meal size;
  - Led to a greater HFAT snack box intake relative to HCHO.

7.3.7 Hunger

Forty-three participants had complete hunger rating data. Overall, fasting hunger was greater post-intervention compared to baseline (F(1,42)=5.75, p=.02). For hunger ratings throughout the day under HFAT and HCHO at baseline and post-intervention (Figure 7-4a), there were no main effects of condition (F(1,42)=0.46, p=.50), exercise training (F(1,42)=0.10, p=.75), interaction between condition and exercise training (F(1,42)=0.001, p=.97) or interaction between condition, exercise training and time (F(7.56,317.44)=0.88, p=.53). There were significant effects of time (F(4.48,188.30)=137.33, p<.001), interaction between condition and time (F(6.95,291.70)=2.23, p=.03), and interaction between exercise training and time (F(6.74,284.12)=2.151 p=.045). Post hoc comparisons revealed that compared to HCHO, hunger in HFAT was lower at 4h and 10h, but was greater at 6h and 7h, and that compared to baseline, hunger was significantly greater at 0h (fasting) and lower at 3h post-intervention. For hunger AUC (Figure 7-4b), there was no effect of condition (F(1,43)=0.03, p=.86), exercise training (F(1,42)=0.94, p=.34) or interaction between condition and exercise training (F(1,42)=0.07, p=.79).

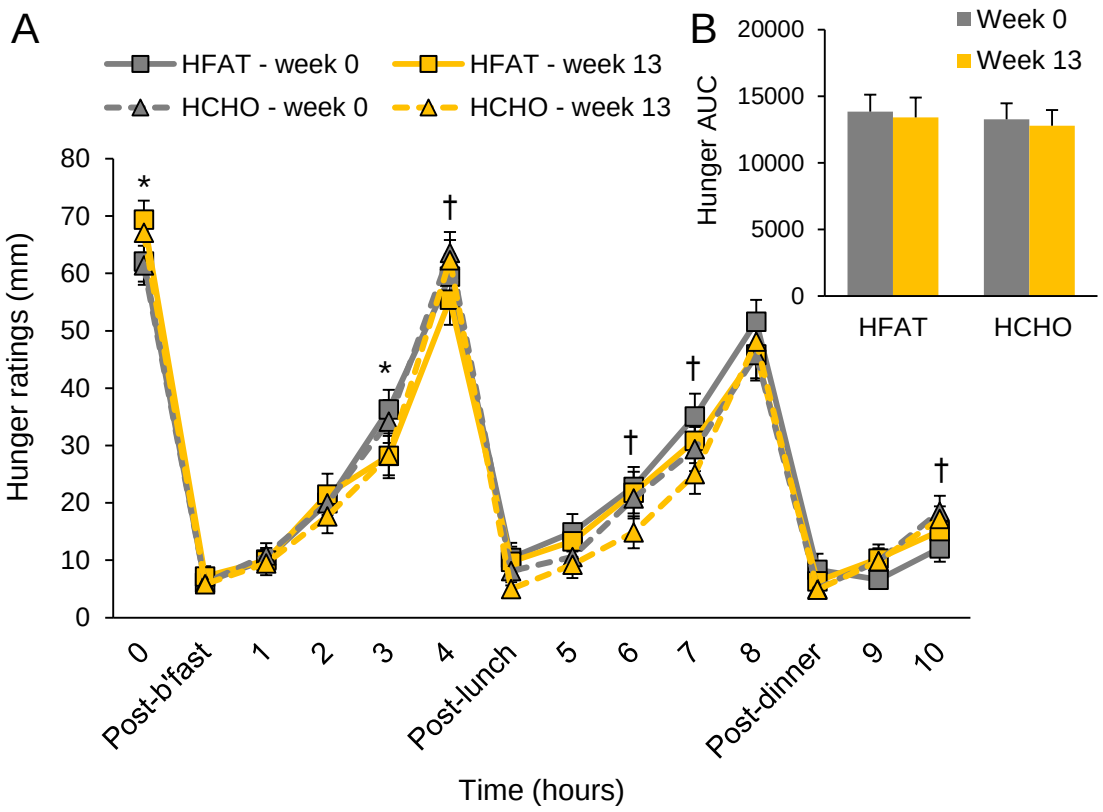

Figure 7-4 Hunger ratings (A) and AUC (B) in HFAT and HCHO conditions at baseline (week 0) and post-intervention (week 13). †HFAT vs. HCHO p<.05; *week 0 vs. week 13 p<.05.

7.3.8 Satiety quotient

Forty-three participants had complete SQ data. Post-breakfast (Figure 7-5), there was a main effect of condition (F(1,42)=5.06, p=.03), with SQ being greater in HCHO relative to HFAT, and a main effect of exercise training (F(1,42)=10.43, p=.002), with SQ being greater post-intervention relative to baseline. There was also a main effect of time (F(1.24,51.88)=59.03, p<.001) and interaction between condition and time (F(1.43,60.32)=12.11, p<.001), with post hoc analyses revealing that SQ was significantly different between HFAT and HCHO post-breakfast and at 1 and 2 hours. There was no interaction between condition and exercise training (F(1,42)=0.05, p=.83), exercise training and time (F(2.34,98.08)=0.87, p=.44) or condition, exercise training and time (F(2.78,116.59)=1.43, p=.24).

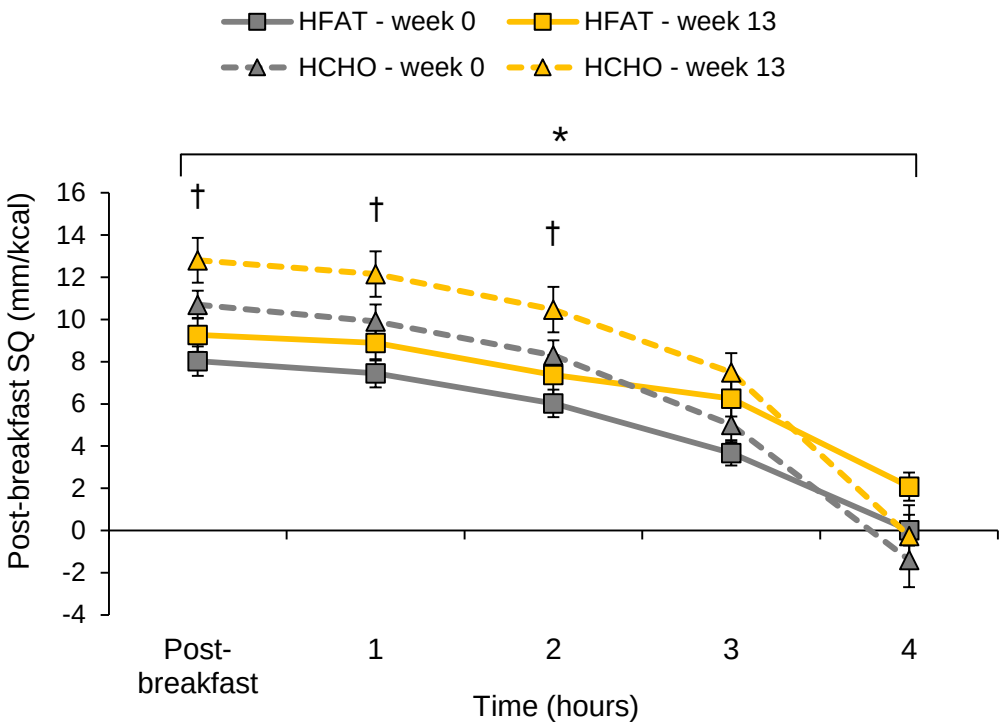

Figure 7-5 SQ post-breakfast in HFAT and HCHO conditions at baseline (week 0) and post-intervention (week 13). †HFAT vs. HCHO p=.03.*Main effect of exercise training (week 0 vs. week 13) p=.002.

Post-lunch (Figure 7-6), there was no main effect of exercise training (F(1,42)=0.03, p=.87), but a main effect of condition (F(1,42)=25.0, p<.001), with SQ being greater in HCHO relative to HFAT, and a main effect of time (F(2.14,90.05)=97.38, p<.001). There was no interaction between condition and exercise training (F(1,42)=0.18, p=.67), condition and time (F(2.75,115.43)=0.83, p=.47), exercise training and time (F(2.45,102.73)=0.30, p=.78) or condition, exercise training and time (F(2.95,123.91)=1.78, p=.16).

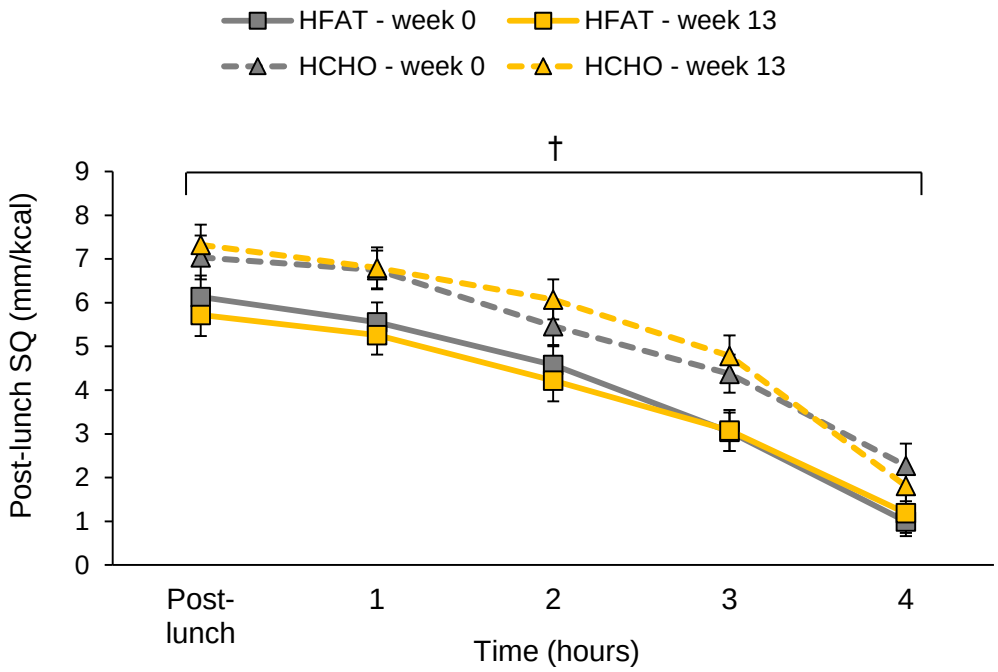

Figure 7-6 SQ post-lunch in HFAT and HCHO conditions at baseline (week 0) and post-intervention (week 13). †Main effect of condition (HFAT vs. HCHO) p<.001.

7.3.9 Food reward

Liking for high-fat foods at the fixed-energy lunch (800kcal for both HFAT and HCHO) was not affected by condition, food consumption or exercise training, nor were there any interactions (all *p*>.33; Figure 7-7).

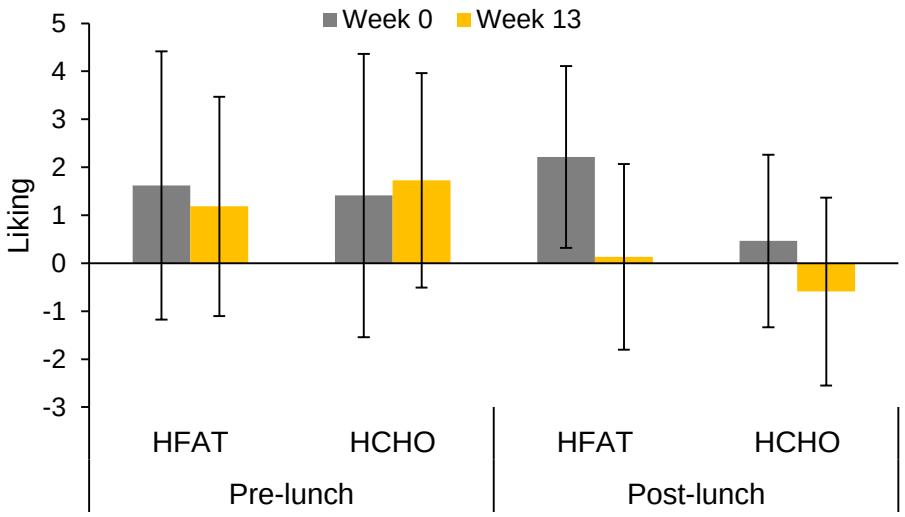

Figure 7-7 Liking pre- and post-lunch in the HFAT and HCHO condition at baseline (week 0) and post-intervention (week 13).

For wanting for high-fat foods at the fixed-energy lunch, there was a main effect of exercise training ($F(1,37)=5.22$, $p=.03$), with overall wanting being significantly lower post-intervention compared to baseline (Figure 7-8). There were no effects of condition, food consumption, or interactions (all *p*>.19).

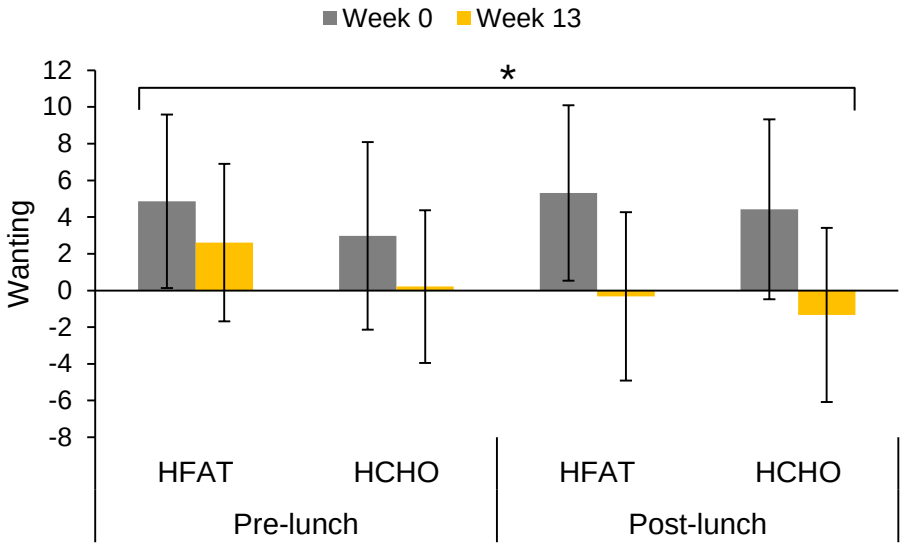

Figure 7-8 Wanting pre- and post-lunch in the HFAT and HCHO condition at baseline (week 0) and post-intervention (week 13). *Main effect of exercise training (week 0 vs. week 13) *p*=.03.

Interim summary 2:

- The exercise intervention:
    - Increased fasting hunger;
    - Increased satiety (SQ) after breakfast in HCHO and HFAT;
    - Reduced the hedonic wanting for high-fat foods.

7.3.10 Are the effects of exercise training on appetite control independent of changes in body composition?

In an attempt to examine whether the impact of exercise training on appetite control is independent of changes in body composition, the analyses in the previous sections were conducted with the change in percentage body fat added as a covariate. The main effects of exercise on the increase in VO_{2max}, reduction in dinner intake, increase in post-breakfast SQ, and reduction in wanting for HFAT foods all remained significant after adding change in percentage body fat as a covariate (p<.05). However, the main effect of exercise training on RMR, fasting appetite-related peptides, eating behaviour traits, and fasting hunger did not remain significant when the change in body fat was added as a covariate (p>.25). The tendency for an interaction between condition and exercise training for the evening snack box intake and total daily energy intake was not apparent after controlling for the change in percentage body fat (p>.30), as well as the reduction in passive overconsumption accounting for changes in RMR (p=.61).

There were, however, interactions between the change in percentage body fat and exercise training for VO_{2max} (p=.04), leptin (p=.03) and ghrelin (p=.04), and an interaction between exercise training, condition and the change in percentage body fat for SQ after lunch (p=.002). To further examine these effects, the participants were divided using a sex-stratified median split of change in percentage body fat based on available SQ values (n=43). The low body fat loss subgroup had 21 participants (14 females, 7 males) and the high body fat loss subgroup had 22 participants (15 females, 7 males). Participant characteristics of these subgroups can be found in Appendix C. These showed that overall, the high body fat loss subgroup had lower BMI, total mass, percent body fat, fat mass, waist circumference and fasting insulin compared with the low body fat loss subgroup independent of the exercise intervention. And in response to the exercise intervention, the high body fat loss subgroup significantly reduced fat mass, increased fat-free mass, tended to increase RMR, increased ghrelin and decreased leptin, whereas these changes were not significant in low body fat loss subgroup (see Appendix C for more details).

Some interesting findings were revealed for SQ after lunch, as shown in Figure 7-9. There was a significant difference between SQ in HFAT and HCHO at baseline for the high body fat loss group (p=.01) and post-intervention in the low body fat loss group (p<.001). In the HFAT condition, SQ increased with exercise training in the high body fat loss group (p=.04), whereas it decreased in the low body fat loss group (p=.007). Post-intervention, SQ in HFAT was greater in the high body fat loss group compared with the low body fat loss group (p=.005).

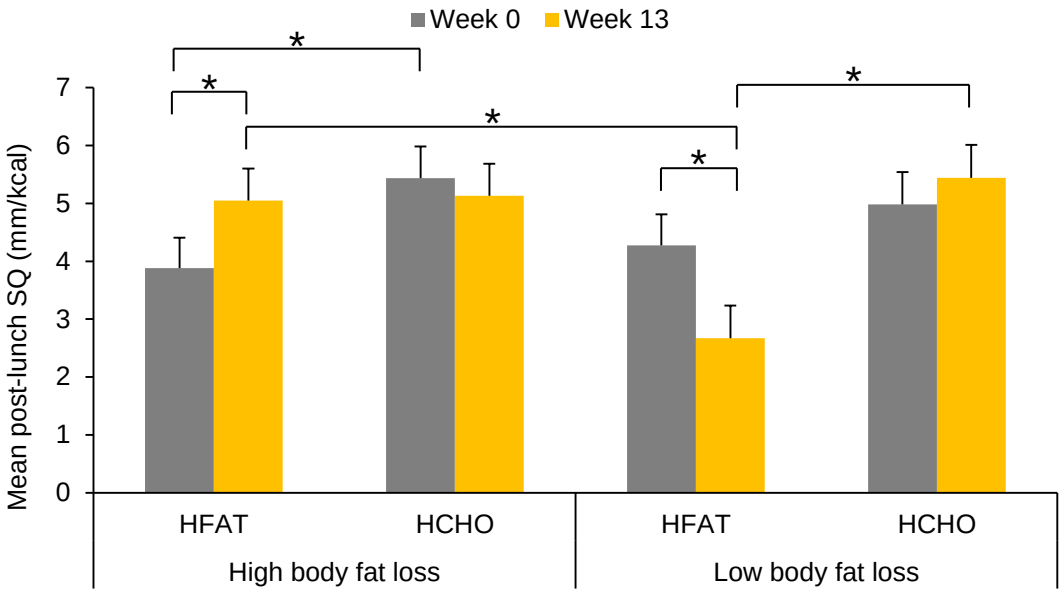

Figure 7-9 Post-lunch SQ (mean of 5 time points) in the HFAT and HCHO conditions at baseline (week 0) and post-intervention (week 13) by sex-specific median split of change in percentage body fat. *Post-hoc analyses p<.05.

Interim summary:

- The exercise intervention, independent of changes in percentage body fat:
  - Reduced dinner intake;
  - Increased post-breakfast SQ;
  - Reduced hedonic wanting for high-fat foods.
- The exercise-induced fat loss may have mediated the:
  - Changes in appetite-related peptides, eating behaviour traits, and fasting hunger;
  - HFAT SQ response post-lunch (increased with high body fat loss and decreased with low body fat loss).

7.3.11 Cross-sectional associations among determinants of appetite control and HFAT and HCHO energy intake

In order to examine the moderating influence of exercise training on associations among determinants of energy intake, baseline and change from baseline analyses were conducted. These evaluated the relationship between a number of hypothesized drivers of appetite, including body composition, appetite-related peptides and food hedonics, and energy intake at the ad libitum meals and for total energy intake.

7.3.11.1 Homeostatic measures

As shown in Table 7-8, at baseline, fat-free mass and RMR were positively associated with HFAT and HCHO dinner meal size and total energy intake, but not with snack box intake. There were no significant associations between percentage body fat and energy intake, but fat mass and BMI were positively associated with HCHO snack box intake. The only peptide associated with energy intake was fasting insulin, which was positively associated with energy intake at the HFAT dinner, and total energy intake in HFAT and HCHO. These associations remained significant when controlling for percentage body fat (all $p \leq .01$).

Table 7-8 Correlations between body composition and physiological measures and HFAT and HCHO energy intake at baseline

	Dinner (kcal)		**Snack box (kcal)**		**Total EI (kcal)**	
	HFAT	**HCHO**	**HFAT**	**HCHO**	**HFAT**	**HCHO**
Total mass (kg)	**.323***	**.400****	.219	**.350***	**.355***	**.486****
Fat mass (kg)	.056	.113	.146	**.315***	.160	.279
Fat-free mass (kg)	**.397****	**.453****	.172	.204	**.348***	**.424****
Body fat (%)	-.204	-.224	.009	.140	-.088	-.047
BMI ($kg \bullet m^{-2}$)	.047	.104	.100	**.343***	.095	.262
RMR ($kcal \bullet 24h^{-1}$)	**.363***	**.468****	.188	.208	**.417****	**.431****
VO_{2max} ($mL \bullet kg^{-1} \bullet min^{-1}$)	**.323***	.179	.160	-.043	.254	.084
Total ghrelin ($pg \bullet mL^{-1}$)[1]	.016	-.144	-.037	-.001	-.029	-.076
Leptin ($ng \bullet mL^{-1}$)[1]	-.201	-.066	-.100	.182	-.223	-.012
Insulin ($ng \bullet L^{-1}$)[1]	**.421***	.310	.193	.260	**.363***	**.394***
GLP-1 ($ng \bullet L^{-1}$)[2]	.170	.160	.063	.277	.133	.219
Total PYY ($ng \bullet L^{-1}$)[3]	.281	.249	.173	.053	.251	.227

[1]n=31; [2]n=23; [3]n=27. *p<.05; **p<.01.

7.3.11.2 Hedonic measures

Because there was no effect of condition on liking and wanting in the fed and hungry states, the mean scores from the HFAT and HCHO conditions were computed for the analysis. There were no associations between food hedonics and energy intake (Table 7-9).

Table 7-9 Correlations between liking and wanting for high-fat foods and HFAT and HCHO energy intake at baseline

	Dinner (kcal)		Snack box (kcal)		Total EI (kcal)	
	HFAT	**HCHO**	**HFAT**	**HCHO**	**HFAT**	**HCHO**
Liking - hungry	.058	.066	-.122	-.048	-.047	-.030
Liking - fed	.075	.087	-.111	.056	-.040	.034
Wanting - hungry	.041	-.023	-.060	.064	.005	.035
Wanting - fed	.102	.106	-.174	-.014	-.036	.026

7.3.12 Associations among exercise-induced changes in the determinants of appetite control and energy intake

To further examine the impact of exercise on appetite control, correlation analyses were conducted between the exercise-induced changes of the hypothesized drivers of appetite (mentioned in the previous section) and the changes in energy intake from baseline to post-intervention.

7.3.12.1 Homeostatic measures

The changes in body composition variables (from baseline to post-intervention) were not associated with the changes in energy intake at dinner, snack box or over the day; however, the change in RMR was positively associated with the change in HFAT dinner intake (see Table 7-10).

The change in fasting total ghrelin was positively associated with HFAT dinner, snack box, and total energy intake, but not with HCHO intake (Table 7-10). These remained significant when controlling for the change in percentage body fat ($p \leq .04$). The changes in fasting insulin and GLP-1 were negatively associated with HCHO energy intake at dinner and over the day (Table 7-10), and remained significant when controlling for change in percentage body fat ($p < .05$).

Table 7-10 Correlations between exercise-induced changes in homeostatic measures and the change in HFAT and HCHO intake from baseline to post-intervention

	ΔDinner (kcal)		**ΔSnack box (kcal)**		**ΔTotal EI (kcal)**	
	HFAT	**HCHO**	**HFAT**	**HCHO**	**HFAT**	**HCHO**
ΔTotal mass (kg)	.038	-.115	-.219	.020	-.158	-.038
ΔFat mass (kg)	.020	-.209	-.247	.007	-.165	-.109
ΔFat-free mass (kg)	.044	.203	.036	.015	-.004	.145
ΔBody fat (%)	-.045	-.275	-.206	.037	-.142	-.125
ΔBMI ($kg \bullet m^{-2}$)	.049	-.134	-.248	.024	-.181	-.051
ΔRMR ($kcal \bullet 24h^{-1}$)	**.294***	.193	-.014	-.135	.088	-.029
ΔVO_{2max} ($mL \bullet kg^{-1} \bullet min^{-1}$)	-.006	.034	-.007	-.059	.063	-.098
ΔTotal ghrelin ($pg \bullet mL^{-1}$)[1]	**.362***	.210	**.510****	.045	**.561****	.134
ΔLeptin ($ng \bullet mL^{-1}$)[1]	-.138	-.093	-.266	.200	-.342	.159
ΔInsulin ($ng \bullet L^{-1}$)[1]	.071	**-.489****	-.010	.001	.072	**-.395***
ΔGLP-1 ($ng \bullet L^{-1}$)[2]	.191	**-.426***	.053	.213	.159	**-.472***
ΔTotal PYY ($ng \bullet L^{-1}$)[3]	-.010	-.267	.173	.019	.078	-.347

[1]*n*=31; [2]*n*=23; [3]*n*=27. *p<.05; **p<.01.

7.3.12.2 Hedonic measures

The exercise-induced changes in hedonic liking and wanting for high-fat foods were not associated with energy intake at any of the meals or over the day, as shown in Table 7-11.

Table 7-11 Correlations between exercise-induced changes in liking and wanting for high-fat foods in the hungry and fed states and the change in HFAT and HCHO energy intake from baseline to post-intervention

	ΔDinner (kcal)		**ΔSnack box (kcal)**		**ΔTotal EI (kcal)**	
	HFAT	**HCHO**	**HFAT**	**HCHO**	**HFAT**	**HCHO**
ΔLiking - hungry	-.136	.164	.018	-.214	-.019	-.118
ΔLiking - fed	.023	.118	-.011	-.128	-.035	-.076
ΔWanting - hungry	-.209	.216	.044	-.122	-.101	.035
ΔWanting - fed	-.100	.113	.156	-.148	.155	-.124

Interim summary 3:

- Baseline fat-free mass and RMR were positively associated with total energy intake and dinner meal size in HFAT and HCHO, but not snack box intake.
- Baseline fasting insulin was positively associated with HFAT meal size and total energy intake in HFAT and HCHO.
- Exercise-induced change in RMR was positively associated with the change in HFAT dinner intake.
- Exercise-induced change in ghrelin was positively associated with the change in HFAT dinner, snack box and total energy intake.
- Exercise-induced changes in insulin and GLP-1 were negatively associated with the change in HCHO dinner and total energy intake.
- There were no association between baseline or exercise-induced changes in hedonic measures and energy intake.

7.4 Discussion

This study examined the impact of a 12-week exercise intervention on homeostatic and hedonic processes of appetite control in inactive overweight and obese individuals. Because of the importance of replication in scientific reporting, this study also allowed for the examination of previous findings of the Leeds group under conditions of HFAT and HCHO food intake. Firstly, this study confirmed the dual-process action of physical activity on appetite control (King et al., 2009). Exercise training in inactive overweight and obese individuals led to an increase in fasting hunger but an increase in satiety after breakfast under both HFAT and HCHO conditions, which has never been reported previously. This demonstrates that the effect of exercise training on satiety is robust and remains under a variety of dietary conditions. Secondly, SQ was lower after consumption of the HFAT meals relative to the HCHO meals, corroborating the study in Chapter 4 (Beaulieu, Hopkins, et al., 2017a) and other research (Hopkins, Gibbons, et al., 2016). This demonstrates that calorie-for-calorie, dietary fat has a weaker satiating efficiency and ability to suppress hunger than carbohydrate (Blundell & MacDiarmid, 1997) – at least over a period of 4 hours (a common postprandial interval). Thirdly, positive associations with fat-free mass and RMR were found with dinner and daily energy intake under both HFAT and HCHO conditions, again in line with prior studies (Blundell et al., 2012a; Caudwell, Finlayson, et al., 2013). The absence of a significant negative relationship between fat mass and energy intake at baseline also supports earlier research in overweight and

obese individuals (Blundell et al., 2012a). In contrast, a significant negative relationship between fat mass and energy intake was observed in non-obese individuals in the previous chapter (Chapter 6) and by Blundell et al. (2015), contributing to the proposition made by these authors that distinct processes control appetite in lean and overweight/obese individuals. Finally, for the first time and contrary to what was hypothesised, this study suggested that physical activity (i.e. exercise training) impacted on satiation with an overall reduction in meal size under both HFAT and HCHO conditions at dinner (91 kcal) in overweight and obese individuals.

7.4.1 The impact of exercise training on the sensitivity of appetite control in overweight and obese individuals

Exercise training induced an increase in both fasting hunger and post-meal satiety after breakfast. The increase in fasting hunger may have resulted from the increase in fat-free mass and RMR (i.e. energy expenditure; Caudwell, Finlayson, et al., 2013), and could be driving the system towards a higher energy intake to match increased energy needs (higher energy flux) as demonstrated in the previous chapter with the positive relationship between physical activity level and energy intake. Despite this rise in fasting hunger and drive to eat, the exercise intervention also increased post-meal satiety after breakfast (i.e. SQ). The increase in satiety response to food consumption was also reflected by an apparent enhanced satiation with an overall reduction in HFAT and HCHO dinner meal size post-intervention. This is in line with the zones of appetite control model introduced in Chapter 1 and discussed throughout this thesis (Blundell, 2011). According to this model, an increase in physical activity in overweight and obese individuals will induce a shift towards the right side (regulated zone) of the J-shape relationship between physical activity level and energy intake. This would at first result in a reduction in energy intake (middle of the J) due to enhanced sensitivity of the appetite control system (i.e. satiation and satiety; further discussed in the following section).

With the reduction in hedonic wanting, disinhibition and binge eating score observed post-intervention, it can be proposed that this shift towards the regulated zone of appetite is accompanied by a reduction in the hedonic states and behavioural traits favouring overconsumption, also contributing to this initial reduction in energy intake. Nevertheless, the absence of a reduction in total energy intake in the HFAT condition further supports the proposition that appetite control may be optimal with HCHO foods. Not only are HFAT (and energy-dense) foods less satiating than HCHO foods, contributing to a passive overconsumption of energy (Blundell & MacDiarmid,

1997), the highly palatable nature of HFAT foods can offset homeostatic satiation and satiety signals (Erlanson-Albertsson, 2005). This could in turn lead to reward-driven (hedonic) rather than homeostatic consumption and constitute a risk factor for overconsumption (Blundell & Finlayson, 2004; Erlanson-Albertsson, 2005). The reduction in hedonic wanting for HFAT foods in the fasted and fed states after exercise training is in contrast to a recent study showing no changes in food hedonics after exercise training in overweight and obese individuals (Martins et al., 2017). Differences in the timing of the LFPQ measurement (morning vs. midday), in the energy expended during the exercise intervention (125-250kcal vs. 500kcal per exercise session) or in the degree of weight loss (1.2% vs. 2.0%) may explain these inconsistencies. However, in the current study, the reduction in hedonic wanting was independent of changes in body composition. Clearly more work is needed to elucidate the impact of different exercise interventions on food hedonics at different times/meals during the day, but the current results demonstrate that a 12-week exercise intervention expending 500 kcal per session reduced the wanting for HFAT foods in the fasted and fed states around midday.

7.4.1.1 The interaction between exercise and body composition in the sensitivity of appetite control

Several adaptations favouring more sensitive appetite control and eating behaviour occurred with exercise training in the current study. These include improvements in body composition, with a reduction in fat mass and an increase in fat-free mass, and supports the argument that physical activity in overweight and obese individuals is beneficial for fat loss (Donnelly et al., 2009). These results also corroborate the cross-sectional studies in this thesis showing that increasing levels of physical activity are associated with lower levels of body fat (Beaulieu, Hopkins, et al., 2017a). Indeed, it is likely that this reduction in body fat is contributing to the increase in the sensitivity of some of the components of the appetite control system. In the current study, the observed changes in fasting appetite-related peptides, and improvements in disinhibition and binge eating score did not remain significant after controlling for body fat, suggesting an impact of weight loss on both physiological and psychological determinants of appetite control. Compensatory adaptations to weight loss towards weight regain may have also led to the increase in fasting hunger and drive to eat. These are beyond the scope of this thesis and have been reviewed elsewhere (King et al., 2012; Melanson, Keadle, Donnelly, Braun, & King, 2013; Riou et al., 2015). Moreover, the increase in fasting ghrelin seen after exercise training was likely due to the weight loss per se, in line with previous studies showing no change in fasting

ghrelin concentrations when exercise training is not accompanied by weight loss (King, Wasse, Stensel, & Nimmo, 2013).

Interestingly, in all participants, SQ post-breakfast increased regardless of the weight loss response to exercise, corroborating previous findings (King et al., 2009); however, it appears that the degree of weight loss mediated the impact of exercise on the SQ at the HFAT lunch. SQ post-lunch (800 kcal of similar energy densities in HFAT and HCHO) increased with those with high body fat loss whereas it decreased with low body fat loss. This finding was unexpected and why this effect was not present at the breakfast meal (varying in energy content and densities) is unclear. It is possible that there are time-of-day differences in the impact of physical activity, body composition and macronutrients on the satiety response to foods (de Castro, 2004). Perhaps an enhancement in the release of fat-stimulated gut peptides or in the central sensitivity to these peptides due to significant body fat loss may have led to this enhanced satiety response to the HFAT meal after exercise training (Schwartz et al., 2000; Stensel, 2010). However, Gibbons et al. (2017) demonstrated that overweight and obese individuals who displayed lower exercise-induced weight loss had an attenuated ghrelin, GLP-1 and total PYY response to food consumption (at HFAT and HCHO meals matched for energy content and density) independent of exercise training (i.e. pre- and post-intervention). These authors suggested that individuals with a weakened postprandial peptide response to food consumption could be more predisposed to exercise-induced compensatory eating, leading to lower body fat loss. As the SQ response to HFAT lunch meal in the current study only differed by the degree of body fat loss after the exercise intervention, it is unknown whether the degree of exercise-induced body fat loss affected the HFAT satiety response or vice versa. Regardless, this interaction between exercise-induced body fat loss and the satiety response to the HFAT lunch meal should be treated with caution before future studies can provide a functional explanation why these interacting variables influence this particular SQ response.

7.4.2 Distinguishing the impact of exercise on satiation and satiety

7.4.2.1 Satiation

Evidence is emerging to propose that physical activity affects the processes of satiation and satiety differently, and that energy density may have a stronger influence on satiation than physical activity in non-obese individuals (Beaulieu, Hopkins, et al., 2017a). It is known that the fat content and energy density of foods have a big impact on satiation and meal size (Beaulieu, Hopkins, et al., 2017a; Blundell & MacDiarmid, 1997; Hopkins, Finlayson, et al., 2016). This was the case in the current study with energy intake being greater in the HFAT compared to the HCHO condition. However, in the current overweight and obese participants, the exercise intervention also led to a reduction in energy intake at the ad libitum dinner meal across both conditions, which suggests an impact on satiation. This main effect may have been driven by the HFAT condition as when the conditions were previously examined separately, exercise-training led to a significant reduction in HFAT but not HCHO meal size (Caudwell, Finlayson, et al., 2013). Given the homeostatic and hedonic determinants of food intake, this reduction in dinner meal size may be associated with enhanced satiation signals and/or the reduction in wanting for HFAT foods. Therefore, in light of these results and the results in the non-obese participants from Chapter 4, more work is required to understand the influence of physical activity and body weight status on the process of satiation and the factors that underpin meal size.

7.4.2.2 Satiety

In contrast to satiation, there is more compelling evidence to suggest that satiety is enhanced with habitual physical activity and exercise training (Beaulieu et al., 2016; Beaulieu, Hopkins, Long, Blundell, & Finlayson, 2017). The exercise intervention increased satiety (i.e. SQ) after breakfast under both HFAT and HCHO conditions. This may have stemmed from greater circulating satiety peptides, such as PYY and GLP-1, which increased with exercise training. While changes in the postprandial action of these peptides may not reflect changes in fasting concentrations as measured in the current study, Martins et al. (2010) found a tendency for elevated postprandial PYY and GLP-1 after 12 weeks of exercise training in overweight and obese individuals. This provides a potential mechanism involved in more sensitive appetite control with chronic exercise (Stensel, 2010).

The lack of observed overall effect of exercise training on satiety at the lunch meal may be due to the type of test meal used (fixed in energy and energy density), which was not ad libitum like the breakfast test meal, which varied in energy content

and densities across conditions. As discussed above, the effect of exercise training and body fat loss on the HFAT SQ response observed at lunch is difficult to interpret and the mechanisms responsible for this effect remain to be elucidated. Nonetheless, with SQ values being greatest post-intervention in the HCHO condition, the combination of regular physical activity and a HCHO diet may be most effective in promoting a strong satiety response to food and optimal appetite control through enhanced peptide signalling (Stensel, 2010) and homeostatic rather than reward-driven feeding (Erlanson-Albertsson, 2005).

The baseline positive association between fasting insulin and energy intake provides further evidence for disrupted postprandial satiety signalling with increasing fat mass in inactive individuals, in contrast to previous research that found a negative association with fasting and postprandial insulin and food intake in lean individuals (Speechly & Buffenstein, 2000; Verdich et al., 2001). But interestingly, in the current study, the change in fasting insulin with exercise training was negatively associated with the change in meal size and daily energy intake in the HCHO condition only. This suggests that exercise training may have enhanced the central inhibitory role of insulin on food intake and/or the mediating role of insulin in the postprandial secretion of GLP-1 or other satiety peptides (Morton et al., 2006; Schwartz et al., 2000). There is evidence in obese rodents that physical activity may restore the central anorectic action of insulin (and leptin) on food intake via cytokines released with exercise, such as IL-6 or IL-10, acting directly on the hypothalamus (Ropelle et al., 2010). A negative association between the change in fasting GLP-1 and HCHO dinner and daily energy intake was also revealed, providing more support for the role of GLP-1 in the enhancement of satiety with exercise as proposed by Stensel (2010), and in line with Martins et al. (2010). Therefore, physical activity in overweight and obese individuals may enhance satiety both centrally and peripherally, through enhancing central insulin and leptin sensitivity and alterations in the release of gut peptides, respectively.

7.4.3 Homeostatic and hedonic determinants of HFAT and HCHO food intake

The weak satiating efficiency, and high palatability (liking) and motivational value (wanting) of HFAT foods have been proposed as contributors to passive overconsumption (Blundell & MacDiarmid, 1997; Bolhuis, Costanzo, Newman, & Keast, 2016). This further emphasises the complex relationships and overlap between homeostatic and hedonic processes of appetite control in explaining susceptibility to overconsumption (Blundell & Finlayson, 2004). As discussed previously, the reduction in hedonic wanting for HFAT foods may have contributed to the reduction in dinner

intake seen post-intervention. These were not correlated but were measured at different meals, which may explain this lack of association or suggests that the reduction in dinner meal size may not have been hedonically-driven. Moreover, paradoxically, the reduction in dinner meal size was followed by a further reduction in HCHO snack box intake but a greater HFAT snack box intake.

After the exercise intervention, there was an overall increase in ghrelin, and a positive association between the change in total ghrelin and HFAT food intake, but not HCHO food intake. This corroborates a rodent study where central injection of ghrelin led to greater intake of a HFAT diet relative to a HCHO diet when presented separately or simultaneously (Shimbara et al., 2004). Furthermore, a role for ghrelin in food reward, especially in the motivation to seek food, has been suggested (Erlanson-Albertsson, 2010; Goldstone et al., 2014). This may explain the difference in HFAT and HCHO snack box intake post-intervention, but is not consistent with the reduction in HFAT dinner intake and wanting for HFAT foods as measured by the LFPQ. However, it is difficult to compare the effects at the dinner and snack box meals as one was consumed within a laboratory setting while the other in free-living conditions; therefore, these may have reflected different appetitive factors or eating behaviours. Indeed, snack box energy intake was not significantly associated with fat-free mass or RMR, which have now been established as reliable homeostatic markers of food intake, as shown in Chapter 6 and in past research (Blundell, Finlayson, et al., 2015). Nevertheless, ghrelin could be a potential determinant of both homeostatic and hedonic appetite control; however, this remains to be elucidated further.

Exercise training in overweight and obese individuals did not reduce passive overconsumption of dietary fat when expressed in grams or calories. However, when considering the influence of physical activity on energy balance through energy expenditure, there was a tendency for passive overconsumption to be reduced when expressed as a percentage of RMR. It is also likely that passive overconsumption would have been reduced when expressed as a percentage of total daily energy expenditure, but this was not measured in the current study. In fact, this was the case in the sub-sample analysis in Chapter 4 when non-obese individuals were classified by objectively measured MVPA. Therefore, despite the increase in energy intake that occurs with HFAT food consumption, physical activity may indirectly help to mitigate episodes of passive overconsumption through its contribution to increasing total daily energy expenditure and impact on energy balance.

7.5 Limitations

While this study measured several homeostatic and hedonic processes of appetite control using a passive overconsumption paradigm, the impact of physical activity on specific mechanisms related to satiation and satiety remain to be fully elucidated. Examining the postprandial peptide response to the test meals could have provided a better understanding of the influence of physical activity on homeostatic appetite control. Other factors could involve gastric emptying, blood flow redistribution, substrate oxidation or fat taste sensitivity (King et al., 2012). The absence of a control group is a limitation to the current study. It would also have been interesting to include a lean group in the exercise intervention to compare the effect of body fat status and physical activity on the homeostatic and hedonic processes of appetite control. And finally, the considerable overlap between homeostatic and hedonic mechanisms influencing satiation and the several adaptations occurring from exercise training make it difficult to tease out specific contributors to the change in food intake observed in the current study.

7.6 Conclusions

In inactive overweight and obese individuals, a 12-week exercise intervention increased fasting hunger, enhanced post-breakfast satiety, and reduced the hedonic wanting for HFAT foods. Physical activity reduced meal size and may have enhanced satiation, but this process may be dependent on the dietary fat content of the foods consumed. This study demonstrated that exercise-training in overweight and obese individuals enhanced appetite control through a favourable impact on homeostatic and hedonic mechanisms, as well as on behavioural traits favouring overconsumption. More research is needed to understand the role of body composition in mediating these effects. Furthermore, physical activity could indirectly mitigate passive overconsumption when considering its impact on energy expenditure.

Chapter summary:

- Exercise training in inactive overweight and obese individuals:
    - Reduced body fat and increased fat-free mass;
    - Reduced HFAT and HCHO dinner meal size (which may be related to enhanced satiation);
    - Concomitantly increased both fasting hunger and post-breakfast satiety;
    - Reduced the hedonic wanting for HFAT foods, disinhibition and binge eating score.
- It is proposed that exercise training is a determinant of appetite control and energy intake in overweight and obese individuals by enhancing the sensitivity of both the homeostatic and hedonic appetite control systems. These effects may be mediated by changes in body composition.
- This study suggests that, in overweight and obese individuals, the appetite control system operates more efficiently:
    - With HCHO foods compared to HFAT foods;
    - Following exercise training (i.e. when physically active).

Chapter 8 – General discussion

8.1 Thesis overview

This thesis investigated the impact of habitual physical activity level in non-obese individuals and exercise training in individuals with overweight and obesity on homeostatic and hedonic appetite processes. Using a multi-level experimental platform that included biological, behavioural and psychological aspects of energy balance, this thesis aimed to clarify the processes involved in the proposed enhancement of the sensitivity of appetite control at higher levels of physical activity and dysregulation of appetite at lower levels of physical activity. It revisited the model of the zones of appetite control across the levels of physical activity proposed by Blundell (2011) based on the classic study by Mayer and colleagues (1956), which suggests that individuals with higher physical activity levels have a better ability to match energy intake to energy requirements, whereas lower levels of physical activity do not appear to downregulate energy intake. In light of the thesis findings and more recent studies, a new perspective of the homeostatic and non-homeostatic contributors to the relationship between physical activity level and energy intake is proposed and discussed in this chapter.

8.1.1 Systematic review of appetite control in active and inactive individuals or in response to exercise training

A systematic review was conducted in Chapter 2 to examine whether physically active individuals have more sensitive control over appetite than their inactive counterparts, and identify whether behavioural or physiological mechanisms underlying any observed differences. The review included a total of 28 studies (cross-sectional and exercise training). The main finding from the review was the demonstration of a J-shape relationship between physical activity level and energy intake (z-scores) from 10 cross-sectional studies in inactive and active individuals. It was the first time this relationship had been reproduced with data from several studies, and confirmed the original findings from Mayer and colleagues (1956). It was also proposed that physically active individuals were more sensitive to the energy content/density of foods based on the studies that used dietary manipulations to test processes of appetite control, namely satiety through preload-test meal paradigms. Inconsistent findings were found for appetite ratings such that no differences in fasting, postprandial or daily ratings of hunger, fullness or other subjective sensations were apparent between

physically active and inactive individuals. Several methodological issues were raised pertaining to the large variations in the definitions of active and inactive individuals, and lack of objective assessment of physical activity level and energy intake. Potential mechanisms involved in the enhancement of appetite control seen at higher levels of physical activity were proposed, such as changes in body composition and appetite-related peptides (episodic and tonic).

8.1.2 Physical activity, satiation and satiety in non-obese individuals

In the systematic review, only one study reported energy intake at meals varying in dietary fat/energy density in response to exercise training in individuals with overweight and obesity (Caudwell, Finlayson, et al., 2013). While not a main outcome of this particular paper, the results suggested that satiation may be enhanced with increasing levels of physical activity as energy intake at a high-fat meal was reduced after exercise training. Therefore, in Chapter 4 (COMPAS), the effect of habitual physical activity level on satiation and the hedonic response to meals varying in dietary fat content was examined in non-obese individuals. This study showed that individuals were susceptible to passive overconsumption at an imposed high-fat meal regardless of physical activity level. No effects of group or dietary fat content were observed in appetite ratings or hedonic response at the ad libitum meal. Sub-analyses based on objectively measured MVPA groups suggested that greater differences in body fat, fasted appetite-related peptides or other determinants of appetite control may be necessary to dysregulate satiation and impact on meal size in response to an increase in dietary fat. In contrast, it may be that energy density has a more potent influence on passive overconsumption and meal size than physical activity level.

As satiation did not appear to be impacted by physical activity level in non-obese individuals in Chapter 4, it was imperative to revisit and confirm, using the Leeds experimental platform, the enhancement in satiety demonstrated in prior studies as reported in the systematic review. Chapter 5 (SCOPE) investigated the effect of habitual physical activity level on satiety and the hedonic response to preloads differing in energy content in non-obese individuals. This study did indeed corroborate previous preload studies using objective classification of habitual physical activity levels and 24-h energy intake, and included the novel aspect of food hedonics. Importantly, the preloads were semi-solid, covertly manipulated, equi-palatable and matched for macronutrient composition. While this study demonstrated similar subjective appetite and hedonic response to the preloads in individuals varying in physical activity levels, the moderate and high active individuals showed enhanced

sensitivity to the nutritional manipulation of the preloads. Unlike their less active counterparts, these individuals adjusted food intake accordingly at the following meal, showing more accurate compensation. However, the effect was only observed at the following meal and no differences in energy intake in response to the preloads were shown at the dinner meal and evening snack box. It was proposed that in these non-obese individuals, the acute compensatory satiety response to the preloads was mediated by homeostatic rather than hedonic mechanisms.

8.1.3 Components of physical activity and appetite control

It was also highlighted in the systematic review that previous research has not examined whether specific components of physical activity are associated with determinants of appetite control or energy intake. This is important to consider, as several methods and definitions were used to classify physically active individuals in the cross-sectional studies in the systematic review. Thus, in Chapter 6 (PALACE), data from Chapters 4 and 5 were pooled to examine the associations among objectively-measured components of physical activity (including daily minutes of physical activity, PAEE and cardiorespiratory fitness), appetite control and energy intake in 70 non-obese individuals. Additionally, the negative association between fat mass and energy intake previously reported in lean individuals (Blundell, Finlayson, et al., 2015; Cugini et al., 1998) was re-examined to investigate whether physical activity level influences this relationship. Significant associations were found between the components of physical activity and meal size, but these were not as apparent with daily energy intake. The association with meal size was strongest with PAEE, and weakened but remained significant when controlling for sex. Moreover, AUC for ratings of fullness, desire to eat and PFC were associated with several components of physical activity.

These results suggest physical activity has a role in the drive to eat and as a determinant of energy intake, and is already a partial response to the AJCN editorial calling for an examination of the effect of PAEE on energy intake (Lam & Ravussin, 2017). The contribution of PAEE to TDEE in these individuals varied from 5% to 43%, which may have considerable implications for appetite control but also help explain why its role as a driver of energy intake is harder to quantify. In fact, the strongest predictors of meal size were found to be TDEE and energy density (the associations between physical activity and TDEE are discussed further below). Interestingly, the strength of the negative association between fat mass and meal size appeared to be moderated by physical activity level as the association was strongest in those with the highest time spent in MVPA. However, given that these individuals also had the least

amount of body fat and were likely more insulin sensitive, it remains unknown if physical activity has a direct effect on this relationship.

8.1.4 Exercise training, satiation and satiety in individuals with overweight and obesity

Chapter 7 (DIVERSE) investigated the effects of a 12-week exercise training intervention in inactive overweight and obese individuals on both the homeostatic and non-homeostatic (food hedonics and behavioural traits) responses to meals varying in dietary fat content. The processes of satiation and satiety were examined, in addition to the impact of body composition (i.e. body fat) on any changes in the determinants of appetite control following the exercise intervention. An apparent impact of exercise training on satiation was found, with a reduction in ad libitum dinner meal size under both HFAT and HCHO meal conditions. The dual-process action was also revealed with an increase in fasting hunger and satiety (post-breakfast SQ) and replicated under both HFAT and HCHO conditions. Additionally, exercise training in these individuals with overweight and obesity reduced the hedonic wanting for high-fat foods, disinhibition and binge eating score, but only the change in hedonic wanting was independent of exercise-induced changes in percentage body fat. Interesting observations were made for the SQ response after consumption of the fixed-energy lunch, which interacted with the change in percentage body fat (SQ increased post-training in those with greater body fat loss and decreased in those with lower body fat loss). While not a direct comparison and using a longitudinal study design, this study provided further insight into the different influences of the homeostatic and non-homeostatic mechanisms of appetite between lean and overweight/obese individuals. In these individuals with overweight and obesity, physical activity affected both satiation and satiety, appetite-related peptides as well as non-homeostatic processes. The fat loss associated with the exercise intervention appeared to mediate the changes in peptides and eating behaviour traits.

8.1.5 Physical activity and the mechanisms of appetite control

All the studies in this thesis examined the potential mechanisms underlying the impact of physical activity on appetite control including body composition and energy expenditure. In Chapter 4 (COMPAS), despite being matched for BMI, the high active individuals had lower body fat than the less active individuals, demonstrating an effect of physical activity on adiposity even in lean individuals. This trend was also observed in Chapter 5 (SCOPE) but did not achieve statistical significance. In Chapter 6

(PALACE), strong negative associations were found between the components of physical activity and adiposity. Chapter 7 (DIVERSE) showed that exercise training in individuals with overweight and obesity led to significant reductions in BMI, total mass, fat mass, and gains in fat-free mass. Overall, this thesis showed clear negative associations between physical activity and body fat.

On the other hand, positive associations were found between physical activity and TDEE. In Chapters 4 and 5 (COMPAS and SCOPE), TDEE in the high active groups was approximately 600 kcal more than the low active groups (with differences in RMR accounting for approximately 100 kcal). This was also reflected in Chapter 6 (PALACE), where physical activity was found to be strongly positively associated with TDEE. Physical activity was also, but to a weaker extent, associated with fat-free mass and RMR; this may be due to the type of physical activities the active individuals were participating in, which tended to be more endurance/aerobic type (e.g. cycling and running) rather than strength/resistance type. This was also the case in Chapter 7 (DIVERSE), where the aerobic exercise training intervention led to a small increase in fat-free mass and a non-significant increase in RMR. Thus, the impact of physical activity on TDEE can largely be attributed to the energy demand stemming from physical activity (i.e. PAEE) itself rather than indirectly through fat-free mass and RMR. And as previously mentioned, PAEE varies widely between individuals depending on their physical activity levels.

In terms of fasted appetite-related peptides, Chapter 4 and 6 (COMPAS and PALACE) examined these in lean individuals and Chapter 7 (DIVERSE) in overweight/obese individuals. In Chapter 4 (COMPAS), differences in insulin, HOMA, leptin and ghrelin were not found in non-obese individuals matched for BMI but when a sub-analysis was conducted in lower and upper tertiles of measured MVPA, trends towards lower insulin, HOMA, leptin and ghrelin were found with increasing physical activity levels but also greater differences in body composition. Chapter 7 (DIVERSE) showed that exercise training in those with overweight and obesity significantly reduced leptin, increased GLP-1, PYY and tended to increase ghrelin. However, these changes were not independent of the exercise-induced fat loss. This suggests that the accumulation of body fat is involved in the dysregulation of appetite, satiety signalling and perhaps satiation at lower levels of physical activity. Interesting associations were found between fasting insulin and energy intake in overweight and obese individuals in Chapter 7 (DIVERSE), with positive associations between insulin and daily energy intake found at baseline. Indeed, insulin has been proposed to exert negative feedback signals to the hypothalamus and that excessive body fat may weaken this signalling (Cummings & Overduin, 2007; Flint et al., 2007; Morton et al., 2006). These

data support this by showing a positive rather than negative association with food intake. After exercise training, however, negative associations were found between the change in insulin and HCHO energy intake, which suggests that exercise training may have enhanced insulin signalling or the signalling of other satiety peptides mediated through insulin sensitivity (Morton et al., 2006; Schwartz et al., 2000). However, no association was found between meal size and insulin in the lean individuals in Chapter 6 (PALACE). Therefore, more work is needed to elucidate the role of physical activity in the relationship between insulin and food intake.

The main findings of the current thesis are summarised in Table 8-1.

Table 8-1 Overview of thesis aims and main outcomes

Thesis aim	Main outcome	Chapter/Publication
Systematically review the literature examining appetite control in active and inactive individuals, and in response to exercise training in inactive individuals.	Replication and confirmation of J-shape relationship between physical activity level and energy intake.	Chapter 2 Beaulieu et al. (2016)
Investigate the effect of habitual physical activity level on satiation and the hedonic response to ad libitum meals varying in dietary fat content in non-obese individuals.	No effect of physical activity level on satiation and food hedonics in response to a passive overconsumption paradigm.	Chapter 4 Beaulieu, Hopkins, et al. (2017a)
Investigate the effect of habitual physical activity level on satiety and the hedonic response to preloads differing in energy content in non-obese individuals.	Moderate and high activate individuals showed enhanced satiety in response to preloads compared with low active individuals, but similar subjective appetite and hedonic response.	Chapter 5 Beaulieu, Hopkins, Long, et al. (2017)

Table 8-1 continued

Thesis aim	Main outcome	Chapter/Publication
Examine the associations among components of physical activity, appetite control and energy intake in non-obese individuals.	The components of physical activity were associated with energy intake but TDEE was the strongest predictor of meal size. Physical activity level may moderate the association between fat mass and meal size.	Chapter 6
Investigate the effect of a 12-week exercise training intervention in inactive overweight and obese individuals on the homeostatic and hedonic response to meals varying in dietary fat content.	Exercise training enhanced satiety, reduced hedonic wanting for high-fat foods, disinhibition and binge eating and impacted on fasting appetite-related peptides, some of which may be mediated by exercise-induced fat loss.	Chapter 7
Examine the potential mechanisms underlying the impact of physical activity on appetite control including body composition, energy expenditure, non-homeostatic processes and fasted appetite-related peptides.	Physical activity was negatively associated with adiposity and positively associated with TDEE. The impact of physical activity on food hedonics, behavioural traits and fasting appetite-related peptides was more prominent with greater body fat.	All chapters Reviewed in Beaulieu, Hopkins, et al. (2017b)

8.2 Towards understanding the role of physical activity in homeostatic and non-homeostatic appetite control

This thesis shed light on the mechanisms contributing to the proposed dysregulation of appetite at lower levels of physical activity and more sensitive appetite control at higher levels of physical activity. It is becoming clearer that these mechanisms may not necessarily be the same along the spectrum of physical activity level and that differences in body composition may also interact with mechanisms of appetite at different levels of physical activity. The systematic review in Chapter 2 showed that chronic exercise may increase the secretion of GLP-1 and PYY (Lund et al., 2013; Martins et al., 2010). In Chapter 7 (DIVERSE), both fasting GLP-1 and PYY increased with exercise-induced fat loss. Therefore, habitual physical activity and exercise may affect appetite-related peptides to strengthen the satiety response to food (Stensel, 2010). Indeed, the studies systematically reviewed in Chapter 2 demonstrated that physically active individuals show better compensation than their less active counterparts following consumption of preloads differing in energy content such that they reduce food intake to offset the difference in energy consumed from the preloads (Beaulieu et al., 2016). Chapter 5 (SCOPE) provided confirmatory evidence for this enhanced satiety response (Beaulieu, Hopkins, Long, et al., 2017). As mentioned in Chapter 5, these improvements in satiety may be associated with exercise-induced adaptations in episodic satiety signalling (Guelfi et al., 2013; Lund et al., 2013; Martins et al., 2010; Martins et al., 2013) or gastric emptying (Horner, Byrne, et al., 2015).

In contrast, Chapter 4 (COMPAS) showed that satiation and passive overconsumption do not appear to be influenced by physical activity level in non-obese individuals (Beaulieu, Hopkins, et al., 2017a). However, in the overweight and obese individuals in Chapter 7 (DIVERSE), exercise training led to a reduction in energy intake at both HFAT and HCHO test meals, which may be interpreted as an enhancement in satiation, but this remains to be fully understood. Habitual physical activity may interact differently with the homeostatic and non-homeostatic mechanisms of appetite in lean and overweight/obese individuals, which may lead to distinct effects on satiation and satiety. As per the J-shape model (Blundell, 2011), an increase in physical activity at lower levels of physical activity and greater body fat may initially reduce energy intake (and overconsumption), which could be related to both enhanced satiation and satiety. However, it is also known that energy density of food has a strong influence on satiation and passive overconsumption (Blundell & MacDiarmid, 1997). Thus, different factors could modulate the appetite processes of satiation and satiety; energy density may more strongly influence satiation whereas physical activity may have more of an effect on satiety signalling.

This thesis also clarified the effects of physical activity on non-homeostatic processes of appetite control. Chapter 7 (DIVERSE) revealed a reduction in hedonic wanting for high-fat relative to low-fat foods, disinhibition and binge eating following exercise training in individuals with overweight and obesity. This corroborates another study that found negative associations between time spent in MVPA and disinhibition and binge eating, but these did not remain significant after controlling for body fat (Myers et al., 2017), and also a study by Shook et al. (2015) who found greater disinhibition in their lowest quintile of MVPA but not when controlling for body weight. Indeed, the aforementioned reduction in disinhibition and binge eating score following 12 weeks of exercise training found in Chapter 7 did not remain significant after controlling for change in body fat. These differences in disinhibition and binge eating were not apparent in the non-obese individuals varying in physical activity levels in Chapters 4 and 5 (Beaulieu, Hopkins, et al., 2017a; Beaulieu, Hopkins, Long, et al., 2017), suggesting the influence of habitual physical activity on eating behaviour traits may be more strongly influenced by body composition. In terms of food hedonics, differences in the rewarding value of foods (liking and wanting) have been observed in lean active compared to overweight inactive males (Horner et al., 2016), but in the non-obese individuals from Chapters 4 and 5 (COMPAS and SCOPE), physical activity level did not influence liking and wanting for high-fat food in the hungry or fed states (Beaulieu, Hopkins, et al., 2017a; Beaulieu, Hopkins, Long, et al., 2017). In inactive individuals with overweight and obesity, 12 weeks of exercise training (125-250 kcal per exercise session) did not affect liking or wanting (Martins et al., 2017), whereas the 12-week intervention from Chapter 7 (DIVERSE) at a higher dose of exercise (500 kcal per exercise session) reduced the hedonic wanting for high-fat food independent of changes in body fat.

8.2.1 Is the impact of physical activity on appetite control moderated by adiposity?

Throughout this thesis, physical activity showed an impact on body composition, which suggests that at lower levels of physical activity, it is likely that greater body fat contributes to the dysregulation of both homeostatic and non-homeostatic appetite control. Indeed, this was seen with the fasting appetite-related peptides in Chapters 6 and 7 (PALACE and DIVERSE), as well as the eating behaviour traits in Chapter 7 (DIVERSE), in which the effects of physical activity were dependent upon body fat. Novel questions regarding the role of body fat in the inhibition of food intake were also posed in this thesis. In Chapter 6 (PALACE), it was found that fat mass was negatively associated with meal size, corroborating prior studies in lean individuals (Blundell,

Finlayson, et al., 2015; Cugini et al., 1998). Interestingly, the findings suggested that the strength of the association between fat mass and meal size may be moderated by physical activity level as the association was strongest in those with the highest time spent in MVPA when divided by sex-stratified MVPA tertiles. As these were exploratory findings, they should be examined and confirmed in future studies. In Chapter 7 (DIVERSE), the interaction between change in body fat with exercise training and SQ at lunch also showed another potential interrelationship between body fat and physical activity in satiety responsiveness. Thus, the satiety signals associated with body fat may be strongest in those with the highest physical activity and lowest amount of body fat. However, the mechanisms responsible for these effects are unknown and whether these stem from a direct effect of physical activity on fat mass or indirectly though other physiological, behavioural or psychological factors remains to be elucidated.

The studies within this thesis examined the impact of physical activity on appetite control in both lean and overweight/obese individuals. In Chapter 4 (COMPAS), there was no impact of physical activity on satiation in lean individuals, whereas in Chapter 7 (DIVERSE), exercise-trained overweight/obese individuals appeared to have enhanced satiation as meal size reduced at the ad libitum evening meal. Whether this is due to physiological signalling per se or to behavioural or hedonic factors is unclear. In terms of satiety, however, low habitual physical activity weakened the satiety response after consumption of a preload even in lean individuals, showing a robust effect of low physical activity. This was also seen in the overweight and obese individuals in Chapter 7 (DIVERSE), who had enhanced satiety (SQ post-breakfast) after exercise training. Moreover, physical activity did not impact food hedonics and eating behaviour traits in the lean individuals in Chapters 4 and 5 (COMPAS and SCOPE), whereas physical activity seemed to have both direct and indirect effects in individuals with overweight and obesity in Chapter 7 (DIVERSE). These findings suggest that the strength of the homeostatic and non-homeostatic inputs vary according to body fat status as well as physical activity level.

8.2.2 A new perspective of the zones of appetite control

This thesis examined several processes and determinants of appetite control occurring at different levels of physical activity that could be contributing to the J-shape relationship found between physical activity level and energy intake (Mayer et al., 1956) and the proposed zones of appetite control (Blundell, 2011). While this model of appetite control was originally based on limited evidence, the systematic review in

Chapter 2 supported this relationship, in addition to another recent study in a large sample of young adults (Shook et al., 2015).

It was first proposed by King et al. (2009) that physical activity enhances appetite control through a dual-process action which increases the drive to eat through greater energy expenditure, but also post-meal satiety. This thesis provides additional evidence to this proposition in both lean and overweight/obese individuals. These processes can be applied to higher levels of physical activity, but how do low levels of physical activity affect appetite control to lead to overconsumption? An important observation in Mayer and colleague's original study that is often overlooked is that individuals with low levels of physical activity also had greater body mass than those with higher levels of physical activity (Mayer et al., 1956). Indeed, this thesis, as well as others (Myers et al., 2017), corroborated this, showing that low levels of physical activity are associated with greater body fat, which has been proposed to weaken satiety signalling (Cummings & Overduin, 2007; Flint et al., 2007; Morton et al., 2006), potentially perpetuating overeating in individuals with excess body fat. Furthermore, it can be suggested that appetite dysregulation at low levels of physical activity is associated with greater non-homeostatic inputs stemming from food hedonics and eating behaviour traits favouring overconsumption. Whether these effects are mediated by higher body fat remains to be fully understood, but were more apparent in individuals with overweight and obesity (Chapter 7) than lean individuals (Chapters 4 and 5). Thus, it is becoming clearer that greater body fat at lower levels of physical activity is also contributing to appetite dysregulation.

Another possible explanation for the increase in energy intake and overconsumption occurring at low levels of physical activity is through the proposed active role of fat-free mass in signalling a drive to overeat (Dulloo et al., 2017). In addition of a passive role for fat-free mass in the tonic drive to eat (via RMR), Dulloo et al. (2017) proposed a more active role for fat-free mass through compensatory feedback signalling in order to restore fat-free mass lost with prolonged physical inactivity and sedentary behaviour. While this active role for fat-free mass was originally based on a dietary weight loss model, Dulloo and colleagues speculated it could apply to highly physically inactive and sedentary individuals.

In light of the results of the current thesis, it can be proposed that in addition to individuals in the non-regulated zone having weakened satiety signalling, excess body fat in this zone may also amplify non-homeostatic inputs favouring overconsumption. In contrast, individuals in the regulated zone with higher levels of physical activity have enhanced postprandial sensitivity, allowing for energy intake to be better matched to energy requirements in response to hunger and satiety signals at higher absolute

levels of energy intake and expenditure. Their energy intake is a function of the relative balance between a stimulatory and inhibitory action. These processes are demonstrated in an updated perspective of the zones of appetite control in Figure 8-1.

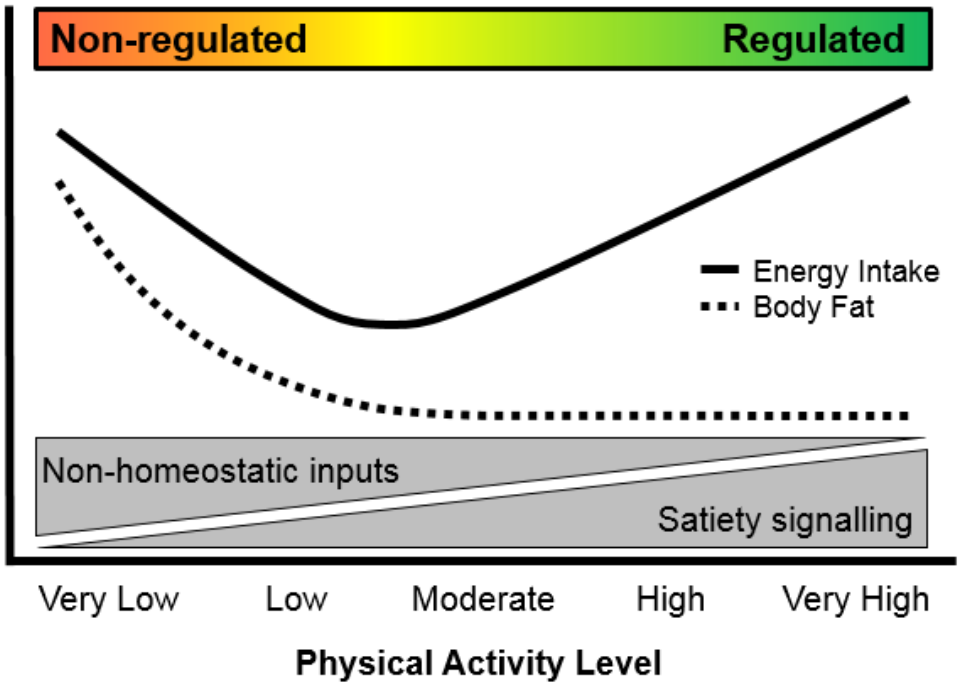

Figure 8-1 An updated perspective of appetite control along the spectrum of physical activity level based on the study by Mayer et al. (1956) and Blundell (2011). Individuals with non-regulated appetite have lower levels of physical activity, higher body fat, greater non-homeostatic influences favouring overconsumption and weaker satiety response to food. Those with regulated appetite have higher levels of physical activity, lower body fat, increased drive to eat and enhanced satiety response to food.

8.2.3 Interaction between physical activity level, appetite control and diet composition: impact on energy balance

Whether being habitually physically active enhances the response to dietary manipulations was also of interest in this thesis to examine the sensitivity of appetite control but also in its overall effect on energy balance. As discussed previously, Chapter 4 (COMPAS) showed that physically active individuals were also prone to acute passive overconsumption with an imposed high-fat meal (Beaulieu, Hopkins, et al., 2017a). In addition, in Chapter 5 (SCOPE), while individuals with higher levels of physical activity were found to be sensitive to the acute nutritional manipulation of preloads varying in energy content by reducing energy intake at the following meal,

objectively-measured daily energy intake (including the preload) was greater after the HEP regardless of physical activity level, demonstrating an effect of passive overconsumption (Beaulieu, Hopkins, Long, et al., 2017). Others have shown that active individuals may compensate beyond the immediate meal following intake of a HEP, attenuating the risk of overconsumption, but this was measured with food records and daily energy intake including the preload was not reported (Martins et al., 2013; Martins, Truby, et al., 2007; Van Walleghen et al., 2007). The long-term compensatory response to high energy density food consumption in physically active individuals is unknown. However, the greater energy expenditure associated with physical activity may be helpful in mitigating episodes of overconsumption and fluctuations in energy intake over time (Hill, 2006; Hume et al., 2016).

8.3 Methodological considerations

The use of a multi-level experimental platform throughout this thesis permitted the examination of several dimensions of appetite control within an energy balance framework (Caudwell et al., 2011). Specifically, each study included measurements such as energy intake, appetite ratings, body composition, energy expenditure, food hedonics, and eating behaviour traits to clarify the role of physical activity in these several determinants of appetite control. While more focus was given on the homeostatic mechanisms, the non-homeostatic processes were also reported and acknowledged, providing a well-rounded view of the influence of physical activity on appetite control.

In Chapters 4 to 6, habitual physical activity was objectively measured using a validated multi-sensor accelerometry device (SWA), which was a major limitation of previous research on habitual physical activity as highlighted in the systematic review in Chapter 2 (Beaulieu et al., 2016). It is important to consider that this multi-sensor device uses proprietary algorithms to quantify physical activity and energy expenditure, thus the data are dependent upon the validity of these algorithms. However, they have previously shown good agreement with the doubly labelled water technique, recognized as the gold standard for the measurement of free-living energy expenditure (Johannsen et al., 2010; St-Onge et al., 2007). The SWA was not worn in water so any swimming or water-based activities were not captured by the device (but recorded in an accompanying log), in addition to not being able to differentiate between structured exercise bouts and non-structured physical activities of daily living. Nevertheless, as the SWA was worn continuously throughout the day/night (except when bathing, showering or swimming), the compliance and data obtained from the

participants was generally good (only 5 out of 75 participants in Chapters 4 and 5 combined had invalid SWA data <5 days of <22h/day).

In addition to objective assessment of physical activity, energy intake was also measured in the laboratory rather than self-reported through food records. While laboratory food intake may not necessarily reflect habitual and real-world consumption, the importance of sensitive energy intake measurements outweighs the potential bias and underreporting often seen with food records (Dhurandhar et al., 2014). The meals within each study were designed to elicit a response on specific appetite process (satiation or satiety) and were pilot tested. However, the reproducibility of these test meal responses were not examined, but passive overconsumption at a high-fat meal (Blundell & MacDiarmid, 1997) and preload-test meal paradigms (Blundell et al., 2010) have been widely used in past research and effective in measuring the strength of satiation and satiety, respectively. Nevertheless, these acute effects may not represent long-term outcomes; thus, the findings from the current thesis need to be interpreted with caution.

Another reliable measurement used throughout this thesis is visual analogue scales for appetite ratings (Flint et al., 2000). In Chapter 4 (COMPAS), a paper-based version of these scales was utilised as the participants only had a half meal day (breakfast to lunch). This may have impacted on the results but given that there was no manipulation done at breakfast and only 3 ratings completed outside the laboratory, any effect was likely small. In Chapter 5 (SCOPE) and 7 (DIVERSE), a validated hand-held electronic device was used to assess appetite ratings over 10 hours throughout the day (Gibbons et al., 2011). This device ensured the appropriate completion of the ratings as each entry was time-stamped and verified by the experimenter.

In Chapter 4 (COMPAS), it was important to covertly manipulate and match the foods of the HFAT and HCHO meals to reduce potential hedonic, cognitive or behavioural influences. While the dietary fat manipulation between the HFAT and HCHO meals was significant (50% vs. 20%) and the energy density was slightly higher in the HFAT meal (2.00 vs. 1.39 kcal/g), larger differences in energy density as in Chapter 7 (2.76 vs. 1.14 kcal/g) may have had more of an impact on satiation. As proposed in the systematic review, physically active individuals appear to be more sensitive to dietary energy density rather than fat per se (Beaulieu et al., 2016). However, it may also be that energy density has a stronger influence on satiation than habitual physical activity in lean individuals. This enhanced sensitivity may also only relate to the energy density/content of prior food intake (i.e. satiety).

In Chapter 5 (SCOPE), the macronutrient composition of the preloads were matched, thus only the energy density/content was manipulated. Considering the

differences in physical activity levels and TDEE between the groups, it can be argued that a preload calibrated to RMR or energy needs as with the breakfast meal (25% of RMR) may have been more physiologically appropriate. However, as prior studies showing more accurate compensation at higher physical activity levels used fixed rather than individually calibrated preloads (Long et al., 2002; Martins et al., 2013; Martins, Truby, et al., 2007; Sim et al., 2015; Van Walleghen et al., 2007), a fixed preload design was chosen. As the satiety response to an individually calibrated preload remains unknown, further research comparing this to a fixed preload is warranted. Additionally, a semi-solid preload in the form of a porridge snack was preferred over a liquid milkshake for its potentially stronger satiety response. Indeed, main effects of preload consumption were found in terms of hunger sensations, food hedonics and energy intake, but only physical activity level interacted with energy intake. This suggests the involvement of a homeostatic rather than a hedonic mechanism, and measurement of postprandial satiety peptides could have provided better insight into this effect.

Given that participants in Chapters 4 and 5 (COMPAS and SCOPE) were lean, it could be argued that their level of physical activity may not have been truly considered as inactive and as low as individuals with overweight and obesity. This was reflected by their measured total daily MVPA, which on average ranged between 80 to 100 minutes per day, which could be considered as relatively active. These individuals could therefore be positioned in the middle of the J-shape relationship (low to moderate physical activity levels). Perhaps lower levels of physical activity may have been required to affect satiation in Chapter 4, but even in lean relatively active individuals, an effect of lower physical activity was found on satiety in Chapter 5. Moreover, it is difficult to compare the minutes of physical activity measured by the SWA with general physical activity recommendations since it cannot distinguish between structured (i.e. exercise) and non-structured physical activities of daily living. According to a recent analysis comparing data obtained from physical activity sensors similar to the SWA with current physical activity guidelines, the amount of total daily MVPA (through structured and non-structured physical activity) to achieve physical activity guidelines (PAL of 1.75) is approximately 140 minutes of total MVPA per day (Thompson, Batterham, Peacock, Western, & Booso, 2016). Only the participants classified as high active in Chapters 4 and 5 achieved this threshold, with total daily MVPA being 182 and 174 minutes, respectively.

Prior to the laboratory experimental sessions in Chapters 4 and 5 (COMPAS and SCOPE), diet and physical activity were standardised such that participants recorded their food intake and ate similarly before each test day in addition to

refraining from exercise for at least 24h. Providing an actual standardised diet prior to testing may have strengthened the results. It also important to consider that imposing inactivity in the physically active individuals may have also affected their appetite processes. There could be a cumulative effect of acute exercise on appetite control in habitually active individuals that is not captured when inactivity is imposed in these individuals. However, as the purpose of the current thesis was to examine habitual physical activity levels and not acute effects of physical activity per se, the additional control obtained by limiting physical activity before and during the experimental session was needed. In Chapter 7 (DIVERSE), the exercise training intervention was supervised, performed within the Human Appetite Research Unit and each session recorded and monitored for compliance. However, the behaviours of the participants outside the laboratory during the intervention were not monitored. Changes in diet and other components of physical activity during the intervention may have impacted the outcomes, but as the original purpose of this study was to examine drivers of compensatory eating behaviours during exercise training and individual variability in exercise-induced weight loss, it was intended for diet to vary freely between individuals.

Potential sex differences in the effect of physical activity on appetite control were mentioned in the systematic review, but the experimental trials did not examine any sex-based differences. While not reported in the current thesis, exploratory analyses in the COMPAS study (Chapter 4) did not find any evidence of sex differences in passive overconsumption. Such analyses were not examined in Chapter 5 (SCOPE) due to the low number of male participants within each group (n=3 to 4). Understanding the impact of sex (or individual differences) on homeostatic and non-homeostatic appetite control may help tailor physical activity interventions or target specific behaviours alongside physical activity for optimal appetite control. The menstrual cycle of female participants was also not considered and may have impacted on the appetite responses. Specifically, in Chapter 7 (DIVERSE), it was not possible to time menstrual cycle around the several test days in line with the beginning and the end of the 12-week intervention.

In Chapter 4 (COMPAS), several plasma samples were below detection levels during the analysis of acylated ghrelin, which may have been due to the protease inhibitor used during the blood sampling process. Aprotinin was added to the whole blood to prevent degradation of acylated ghrelin shortly following the venepuncture (~1 minute) rather than having it directly in the blood tube, which may have affected the results. Other inhibitors such as p-hydroxymercuribenzoic or treatment of the plasma with hydrogen chloride following centrifugation may also have improved the outcomes

(Broom et al., 2007). In Chapter 7 (DIVERSE), the missing values for GLP-1 and total PYY were also due to being below detection levels for the assay; however, concentrations of these satiety peptides are expected to be low during fasting.

Finally, the inter-relationships that exist between physical activity, sedentary behaviour, body composition and energy expenditure make it difficult to isolate which specific component associated with physical activity is contributing to the sensitivity of appetite control. Their individual influences on particular homeostatic or non-homeostatic processes also remains to be fully elucidated. Nevertheless, classifying physical activity level according to MVPA showed a clear impact on appetite control in Chapter 5 (SCOPE), as well as the higher intensity exercise-training intervention (70% HR_{max}) in Chapter 7 (DIVERSE). Therefore, MVPA appears to be a viable target to benefit appetite control, in line with current WHO guidelines promoting MVPA (World Health Organization, 2017). However, future studies could shed light on these interactions, discussed in Section 8.5.

8.4 Overall implications for appetite control across the levels of physical activity

At very low levels of physical activity, the impact of physical activity on the mechanisms of appetite control has implications for individuals with overweight and obesity wishing to lose fat mass through exercise, as large variability in the individual response to exercise interventions have been observed (King et al., 2009; King et al., 2008). These varying responses in fat loss to exercise training suggest that some individuals compensate for the increase in physical activity (and energy expenditure) through greater food intake or other mechanisms impacting on energy balance, minimizing the effect of exercise on fat loss. In both those susceptible and resistant to exercise-induced weight loss, hunger and the strength of satiety were found to be enhanced with exercise training, showing a robust effect of the dual-process action of physical activity on appetite control; however, the increase in hunger was greater in those resistant to weight loss (King et al., 2009). Furthermore, certain baseline (pre-intervention) characteristics of appetite may predict the susceptibility to exercise-induced weight loss such as the hedonic response to acute exercise (Finlayson, Caudwell, et al., 2011) and the peptide response to food consumption (Gibbons et al., 2017), which is of interest as this may help personalise interventions to promote successful fat loss with exercise. It is important to acknowledge that in the individuals considered as resistant to exercise-induced weight loss, other markers of health were improved, such as cardiorespiratory fitness, blood pressure, waist circumference and

positive mood (King et al., 2012), highlighting the importance of habitual physical activity for general health outcomes. In these individuals, it may be that dietary recommendations in addition to exercise training would be more beneficial for fat loss.

In lean individuals with low to moderate levels of physical activity, such as in Chapter 5 (SCOPE), signs of appetite dysregulation and weakened satiety were present as these individuals did not compensate appropriately for the differences in energy content between the preloads. Therefore, this suggests that these individuals could be prone to further appetite dysregulation, overconsumption and weight gain over time if their physical activity levels stay low. In contrast, at higher levels of physical activity, with both the drive to eat and satiety being enhanced, overconsumption and weight gain could occur if food choices are kept mainly energy dense. Additionally, these individuals may also need to exert some dietary restraint, as suggested in Chapter 4 (COMPAS) and in previous exercise-training studies (Bryant et al., 2012), to control food intake and body weight in the current obesogenic food environment.

Given the aforementioned evidence on passive overconsumption with high-fat/energy dense foods, in the general population, higher levels of habitual physical activity in conjunction with a healthy diet lower in energy density appear to be optimal for appetite control and energy balance. Therefore, the focus of health practitioners should not only be given on the energy intake or energy expenditure side of energy balance as they interact with each other at all levels of physical activity.

8.5 Further research

The work stemming from this thesis has led to a number of peer-reviewed journal articles (see Page ii). An invitation to publish in the Society for the Study of Ingestive Behavior Special Issue of Physiology & Behavior also led to a publication which reviewed the work from this thesis and recent evidence on the topic. In addition to these, it is anticipated that the following papers will be submitted for publication:

- The role of physical activity as a determinant of energy intake and in the relationship between fat mass and meal size (Chapter 6)
- Homeostatic and non-homeostatic responses to a medium-term exercise intervention in individuals with overweight and obesity (Chapter 7)

Furthermore, a number of important questions have arisen from this thesis that remain unanswered. The role and contribution of physical activity in driving food intake is important for future research to clarify as it can make up a significant proportion of TDEE in physically active individuals (Lam & Ravussin, 2017). While the influence of physical activity on some processes of appetite appear to be independent of body fat, more research is required to understand the role of body composition and body fat status in the relationship between physical activity level and appetite control. It was reported in Chapter 6 that physical activity (or factors associated with physical activity) may moderate the relationship between fat mass and energy intake, which is an interesting avenue for future research. As a recent study found that habitual (self-reported) physical activity may differently impact food cravings depending on exercise type and sex (Drenowatz et al., 2017), further research into the effect of various exercise types of physical activity such as endurance, strength and intervals, is required. Moreover, very little is known on how the dose, intensity and timing of habitual physical activity and exercise affect homeostatic and non-homeostatic appetite. Additionally, genes (Dorling et al., 2016), sex (Thackray et al., 2016) and age (Van Walleghen et al., 2007) are other potential moderators of the relationship between physical activity and appetite that need to be examined further. The mechanisms responsible for the apparent enhancement in the satiety response to food consumption in physically active individuals also remain to be fully elucidated, but are likely associated with postprandial satiety signalling. Finally, in light of the research on the interaction between physical activity and dietary manipulations, it is important for future research to take an energy balance perspective to increase our understanding of the complex inter-relationships among physical activity, diet composition, body composition and appetite control.

8.6 Conclusions

Food intake is modulated by several homeostatic and non-homeostatic mechanisms controlling appetite, which, as shown in this thesis are impacted by physical activity level. This thesis provides further evidence that the relationship between physical activity level and energy intake is J-shaped, with individuals with low levels of physical activity being in a non-regulated zone of appetite whereas those with higher levels of physical activity operating in a regulated zone with more sensitive appetite control. It was also found that body fat varied according to physical activity level. This may impact the sensitivity of satiety signals, hedonic states (e.g. wanting) and eating behaviour traits (e.g. disinhibition, binge eating) favouring overconsumption at lower

levels of physical activity, but remains to be fully understood. This thesis corroborated the suggestion that physical activity enhances the homeostatic mechanisms of appetite via a dual-process action of increased drive to eat from greater energy expenditure, together with an enhanced satiety response to food, perhaps through more sensitive postprandial signalling. These processes could generate a better adjustment of energy intake to energy expenditure in response to hunger and satiety signals at higher levels of physical activity. However, special attention needs to be given to diet composition, with a high-fat energy-dense diet leading to a passive overconsumption of energy among individuals at all levels of physical activity. Importantly, the strength of the various mechanisms and processes impacted by physical activity will likely vary between individuals, highlighting the need to recognise that the effect of physical activity on the sensitivity of appetite control is not a case of ‘one size fits all’.

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Appendix A

A.1 Systematic review detailed search strategy

OvidSP Medline

1. Motor activity/
2. Exercise/
3. Oxygen consumption/
4. Physical Fitness/
5. Exercise tolerance/
6. Exercise test
7. Physical endurance
8. Physical activity
9. Physical performance
10. Aerobic
11. Aerobic capacity
12. Training
13. Maximal VO2
14. Physical capacity
15. or/1-14
16. Appetite/
17. Feeding behavior/ or food preferences/
18. Hunger
19. Satiety
20. Satiation
21. Fullness
22. Motivation to eat
23. Food choice
24. Food selection
25. Desire to eat
26. Palatability
27. Food reward
28. Hedonic
29. Liking
30. Wanting
31. or/1-15
32. Energy intake/
33. Diet/
34. Calori* intake
35. Food intake
36. Meal size
37. Energy compensation
38. Energy density
39. Dietary proteins/ or dietary fats/ or dietary carbohydrates/
40. Macronutrient
41. or/1-9
42. Gut hormone*
43. Gut peptide*
44. Peptide YY or PYY
45. Ghrelin
46. Glucagon-like peptide-1 or GLP-1
47. Pancreatic polypeptide or PP
48. Leptin
49. Insulin
50. Cholecystokinin or CCK
51. Or/ 1-9
52. 41 OR 51
53. 31 AND 52
54. 15 AND 53
55. Limit 54 to (English language and humans and 19-64 years)

A.2 Systematic review risk of bias assessment

	Sequence generation	Allocation concealment	Blinding participants and personnel	Blinding outcome assessors	Incomplete outcome data	Selective outcome	Other source of bias
Cross-sectional studies							
Apolzan et al. (2009)	N/A	N/A	Unclear risk	Unclear risk	Low risk	Low risk	High risk
Catenacci et al. (2014)	N/A	N/A	Unclear risk	Unclear risk	Low risk	Low risk	High risk
Charlot & Chapelot (2013)	Unclear risk	N/A	High risk	Unclear risk	Low risk	Low risk	High risk
Deshmukh-Taskar et al. (2007)	N/A	N/A	Unclear risk	Unclear risk	High risk	Low risk	High risk
Georgiou et al. (1996)	N/A	N/A	Unclear risk	Unclear risk	Unclear risk	Low risk	High risk
Gregersen et al. (2011)	N/A	N/A	Unclear risk	Unclear risk	Low risk	Low risk	High risk
Harrington et al. (2013)	N/A	N/A	Unclear risk	Unclear risk	Low risk	Low risk	High risk
Jago et al. (2005)	N/A	N/A	Unclear risk	Unclear risk	High risk	Low risk	High risk
Jokisch et al. (2012)	Unclear risk	N/A	High risk	Unclear risk	Low risk	Low risk	High risk
Long et al. (2002)	Unclear risk	N/A	Low risk	Unclear risk	Low risk	Low risk	High risk
Lund et al. (2013)	N/A	N/A	Unclear risk	Unclear risk	Low risk	Low risk	High risk
Rocha et al. (2013)	Unclear risk	N/A	High risk	Unclear risk	Low risk	Low risk	High risk
Rocha et al. (2015)	Unclear risk	N/A	High risk	Unclear risk	Low risk	Low risk	High risk
Van Walleghen et al. (2007)	Unclear risk	N/A	High risk	Unclear risk	Low risk	Low risk	High risk

A.2 Risk of bias assessment (continued)

	Sequence generation	Allocation concealment	Blinding participants and personnel	Blinding outcome assessors	Incomplete outcome data	Selective outcome	Other source of bias
Exercise-training studies							
Alkahtani et al. (2014)	Unclear risk	N/A	High risk	Unclear risk	Low risk	Low risk	High risk
Bryant et al. (2012)	N/A	N/A	Unclear risk	Unclear risk	Unclear risk	Low risk	High risk
Caudwell et al. (2013)	N/A	N/A	Unclear risk	Unclear risk	Unclear risk	Low risk	High risk
Caudwell et al. (2013)	N/A	N/A	Unclear risk	Unclear risk	Unclear risk	Low risk	High risk
Cornier et al. (2012)	N/A	N/A	Unclear risk	Unclear risk	Low risk	Low risk	High risk
Guelfi et al. (2013)	Unclear risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	High risk
Jakicic et al. (2011)	Unclear risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	High risk
King et al. (2008)	N/A	N/A	Unclear risk	Unclear risk	Low risk	Low risk	High risk
King et al. (2009)	N/A	N/A	Unclear risk	Unclear risk	Unclear risk	Low risk	High risk
Martins et al. (2007)	N/A	N/A	Low risk	Unclear risk	Low risk	Low risk	High risk
Martins et al. (2010)	N/A	N/A	Unclear risk	Unclear risk	Low risk	Low risk	High risk
Martins et al. (2013)	N/A	N/A	Unclear risk	Unclear risk	Low risk	Low risk	High risk
Rosenkilde et al. (2013)	Low risk	N/A	Unclear risk	Unclear risk	Low risk	Low risk	High risk
Shaw et al. (2010)	Low risk	N/A	High risk	Unclear risk	Low risk	Low risk	High risk

A.3 Additional studies published after 15th April 2015

A.3.1 Cross-sectional studies

Table A-1 Cross-sectional studies assessing appetite control in physically active and inactive individuals

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Beaulieu et al. (2017)	Non-obese men and women Active: n = 20 (50% men); age = 30±10 years; BMI = 22.6±1.9 kg/m^2; body fat =19.7±8.2 %; VO_{2max} = 50.5±7.5 mL/kg/min; MVPA = 182±67 min/d Inactive: n = 19 (42% men); age = 30±9 years; BMI = 23.1±2.7 kg/m^2; body fat =25.6±7.1 %; VO_{2max} = 34.7±5.6 mL/kg/min; MVPA = 103±37 min/d	IPAQ and physical activity monitor (SenseWear) Active: ≥4 exercise sessions/wk Inactive: ≤1 exercise session/wk Exercise session: ≥40 min MVPA	Laboratory: fixed breakfast followed by HCHO or HFAT ad libitum meal	Energy intake Hunger, fullness, desire to eat, and palatability, SQ (VAS) Eating behaviour traits and food reward (LFPQ): liking and wanting for high-fat foods pre- and post-lunch	No improvement in satiation or resistance to passive overconsumption of energy in active compared to inactive (both had greater energy intake in HFAT relative to HCHO). No differences in food reward, SQ or appetite ratings between active and inactive.

Table A-1 continued

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Beaulieu, Hopkins, Long et al. (2017)	Non-obese men and women HiMVPA: n = 12 (33% men); age = 39±10 years; BMI = 22.4±2.1 kg/m^2; body fat =22.9±8.0 %; VO_{2max} = 46.4±6.4 mL/kg/min; MVPA = 174±39 min/d ModMVPA: n = 11 (27% men); age = 26±3 years; BMI = 22.7±2.2 kg/m^2; body fat =24.5±8.8 %; VO_{2max} = 43.5±6.8 mL/kg/min; MVPA = 121±15 min/d LoMVPA: n = 11 (27% men); age = 30±11 years; BMI = 23.1±2.9 kg/m^2; body fat =27.6±6.5 %; VO_{2max} = 37.0±7.0 mL/kg/min; MVPA = 83±16 min/d	Tertiles of daily MVPA measured by physical activity monitor (SenseWear)	Laboratory: fixed breakfast, high-energy and low-energy preloads followed by ad libitum lunch, dinner and evening snack box	Energy intake Hunger, fullness, desire to eat, and (VAS) Eating behaviour traits and food reward (LFPQ): liking and wanting for high-fat foods pre- and post-preloads	ModMVPA and HiMVPA reduced ad libitum energy intake at the lunch meal following consumption of the high-energy compared to the low-energy preload, while the LoMVPA group did not. No effect of MVPA group on energy intake at dinner or evening snack box. No differences in food reward or appetite ratings between MVPA groups.

Table A-1 continued

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Horner et al. (2016)	Men Active: n = 22; age = 29±8 years; BMI = 24.5±2.6 kg/m^2; body fat =14.3±5.8 %; VO_{2max} = NR; PA = 709±239 kcal/d Inactive: n = 22; age = 31±9 years; BMI = 27.4±4.2 kg/m^2; body fat =26.2±8.7 %; VO_{2max} = NR; PA = 525±185 kcal/d	Self-report and physical activity monitor (ActiGraph) Active: ≥4 exercise sessions/wk Inactive: ≤1 exercise session/wk Exercise session: ≥40 min moderate to high intensity PA	Laboratory: fixed breakfast followed by lunch meal	Hunger, fullness, desire to eat, and palatability (VAS) Food reward (LFPQ): explicit liking, implicit wanting and food preferences post-breakfast and pre-lunch	No significant differences in appetite and palatability ratings between active and inactive. Liking: when fed, active men had lower liking for high-fat foods, low-fat sweet foods and for foods overall compared to inactive. No differences between active and inactive when hungry. From fed to hungry, active had greater increase in liking for all food categories combined than inactive. Wanting: when fed and hungry, active men had greater wanting for low-fat savoury foods than inactive.

Table A-1 continued

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Shook et al. (2015)	Men and women Group 1: n = 85 (48.2 % men); age = 30±3 years; BMI = 29.6±3.3 kg/m^2; body fat = ~35.8 %; VO_{2max} = NR; MVPA = 15.7±9.9 min/d Group 2: n = 84 (48.8 % men); age = 28±4 years; BMI = 26.8±3.6 kg/m^2; body fat = ~30.9 %; VO_{2max} = NR; MVPA = 39.2±16.2 min/d Group 3: n = 84 (48.8 % men); age = 27±4 years; BMI = 25.2±3.0 kg/m^2; body fat = ~27.7 %; VO_{2max} = NR; MVPA = 63.3±22.4 min/d Group 4: n = 84 (48.8 % men); age = 28±4 years; BMI = 23.5±2.5 kg/m^2; body fat = ~23.7 %; VO_{2max} = NR; MVPA = 95.4±27.8 min/d Group 5: n = 84 (48.8 % men); age = 26±4 years; BMI = 23.0±2.3 kg/m^2; body fat = ~21.0 %; VO_{2max} = NR; MVPA = 174.5±60.5 min/d	Physical activity monitor (SenseWear) Quintiles based on minutes of daily MVPA	Free-living	Energy intake (reported from 24-h dietary recall and calculated with equation based on changes in body composition) Restraint, disinhibition and susceptibility to hunger (TFEQ) Craving control (Control of Eating Questionnaire)	No group differences in reported or calculated energy intake. Trend towards increasing energy intake with increasing physical activity level except for group 1 (J-shape relationship). Greater disinhibition in group 1 compared to the other groups. Tendency for disinhibition to be greater after adjustment for body weight. Group 1 had higher craving scores for savoury foods compared to group 5.

Table A-1 continued

Study	Participants	Physical activity status	Setting	Outcome measures	Results
Tucker (2016)	Middle-aged women n = 300; age = 40±3 years; BMI = 23.7±3.3 kg/m^2; body fat = NR; VO_{2max} = NR; PA = 2,764,109 ± 861,954 activity counts/wk	Physical activity monitor (ActiGraph) Quartiles of physical activity counts/wk Low (Q1; n=75): <2,115,191 counts/wk Moderate (Q2 &Q3; n=150): >2,115,191 to ≤3,229,029 counts/wk High (Q4; n=75): >3,229,029 counts/wk	Free-living	Energy intake (7-day weighed food diary)	Women in high physical activity category consumed more than women in low and moderate categories.

A.3.1.1 Participant characteristics: Standardized body fat

When standardized body fat was plotted according to physical activity level similar to energy intake as described in Chapter 2 (Figure A-1), a negative relationship appeared. One-way ANOVA confirmed a main effect of graded physical activity level on percentage body fat z-score ($F(3,21)=70.31$, $p<.001$). Post hoc trend analyses revealed significant effects for linear ($F=101.77$, $p<.001$) and curvilinear (quadratic) ($F=26.65$, $p<.001$) functions.

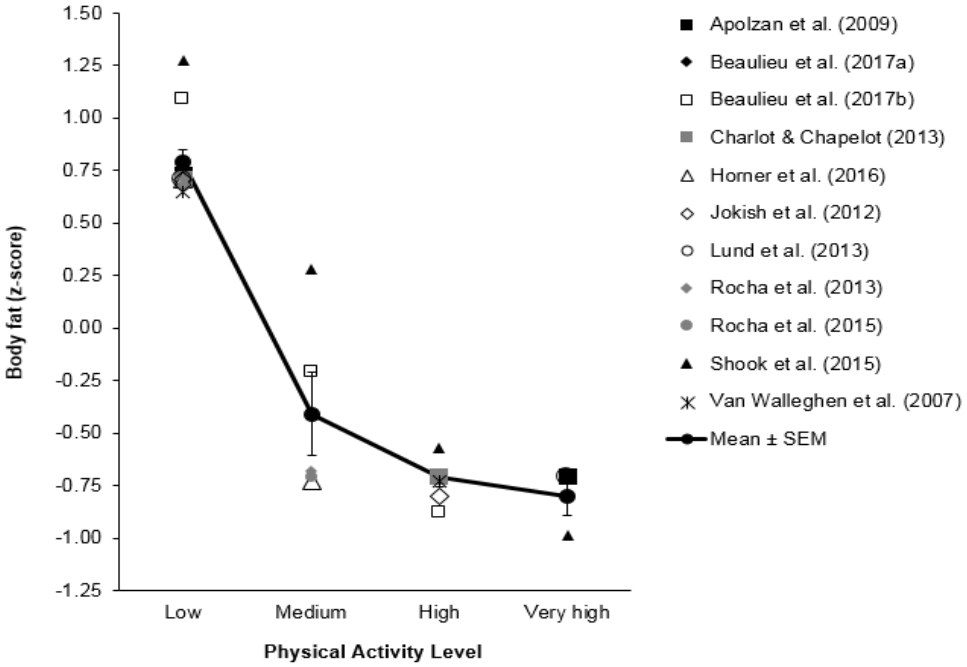

Figure A-1 Standardised body fat percentage by physical activity level from the 11 cross-sectional studies reporting body fat ($n=25$ data points). Trend analysis confirmed significant linear and quadratic relationships ($p<.001$) between graded physical activity level and body fat percentage z-scores. Black line indicates mean of the z-scores.

A.3.1.2 Study results: Standardized energy intake

Similar to Chapter 2, the updated relationship between physical activity level and energy intake also revealed J-shaped curve (Figure A-2). One-way ANOVA confirmed a main effect of graded physical activity level on energy intake z-score ($F(3,33)=6.10$, $p=.002$). Post hoc trend analyses revealed significant effects for linear ($F=15.63$, $p<.001$) and curvilinear (quadratic) ($F=7.07$, $p=.01$) functions.

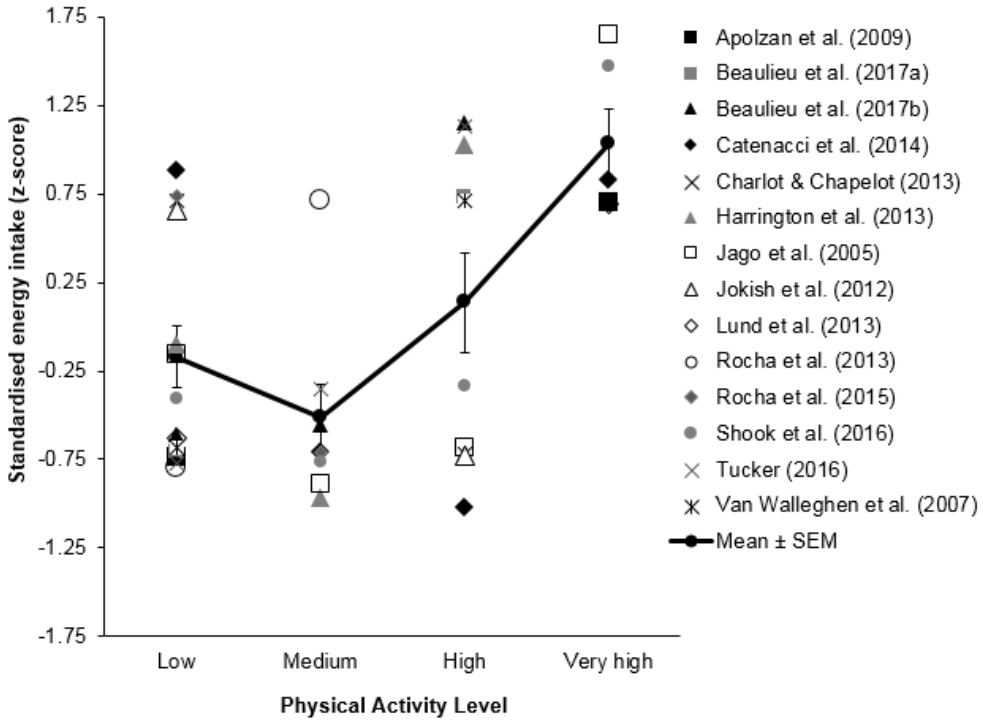

Figure A-2 Standardised energy intake by physical activity level from the 14 cross-sectional studies reporting energy intake ($n=37$ data points). Trend analysis confirmed significant linear ($p<.001$) and quadratic ($p=.01$) relationship between graded physical activity level and energy intake scores. Black line indicates mean of the z-scores, *SEM* standard error of the mean.

A.3.2 Exercise-training interventions

Table A-2 Studies investigating the effect of exercise training on appetite control in previously inactive individuals

Study	Participants	Training intervention	Setting	Outcome measures	Results
Beaulieu et al. *Chapter 7*	Overweight and obese men and women n = 46; age = 43±8 years; BMI baseline = 30.5±3.8 kg/m^2; BMI post = 29.9±4.0 kg/m^2; body fat baseline = 40.0±7.6 %; body fat post = 38.1±8.2 %; VO_{2max} baseline = 33.4±8.1 mL/kg/min, VO_{2max} post = 39.1±6.8 mL/kg/min	12 wk supervised aerobic exercise 5d/wk (500kcal at 70% HR_{max})	Laboratory: HFAT and HCHO probe days.	Food intake (Self-determined fixed breakfast, fixed energy lunch and ad libitum dinner and evening snack box) Hunger (VAS), SQ Liking and wanting (LFPQ), Restraint, disinhibition (TFEQ), binge eating	Reduction in HFAT and HCHO dinner meal size Increase in fasting hunger and post-breakfast SQ under both HFAT and HCHO Reduction in hedonic wanting for HFAT foods, disinhibition and binge eating score.

Table A-2 continued

Study	Participants	Training intervention	Setting	Outcome measures	Results
Garnier et al. (2015)	Postmenopausal women n=156; age = 60±0.4 years; BMI baseline = 30.0±0.4 kg/m^2; BMI post = 39.5±0.3 kg/m^2; body fat baseline = ~44.7%; body fat post = ~43.3%; VO_{2max} baseline = 18.4±0.5 mL/kg/min; VO_{2max} post = 25.8±0.4 mL/kg/min	16 wk supervised walking 2d/wk (45 min at 60% heart rate reserve) + 1 d/wk unsupervised walking (45 min at 60% heart rate reserve)	Free-living	Energy intake and food group consumption (3-day food record)	No significant change in total energy intake after post-intervention. % energy from carbohydrate decreased and % energy from protein increased after training. Reduction in daily servings of fruit and sweet and fatty foods, and increase in daily servings of oil post-intervention.
Gibbons et al. (2017) Exercise groups	Overweight and obese men and women Responders: n = 8 (25% male); age = 46±8 years; BMI baseline = 29.5±2.5 kg/m^2; BMI post = 28.3±3.1 kg/m^2; body fat baseline = ~39.6 %; body fat post = ~36.3 %; VO_{2max} baseline = 29.4±10.2 mL/kg/min, VO_{2max} post = 40.9±8.8 mL/kg/min Non-responders: n = 8 (38% male); age = 45±5 years; BMI baseline = 30.1±3.4 kg/m^2; BMI post = 30.1±3.7 kg/m^2; body fat baseline = ~39.3 %; body fat post = ~38.7 %; VO_{2max} baseline = 36.6±8.8 mL/kg/min, VO_{2max} post = 39.9±5.9 mL/kg/min	12 wk supervised aerobic exercise 5d/wk (500kcal at 70% HR_{max})	Laboratory: HFAT and HCHO breakfasts followed by test meal	Hunger, fullness and desire to eat (VAS) Energy intake (1 ad libitum meal) Insulin, total and acylated ghrelin, GLP-1, total PYY and CCK	No difference in fasting peptide concentrations between responders and non-responders in response to exercise training. No effect on insulin or CCK. Responders showed greater postprandial suppression of acylated ghrelin compared to non-responders (except after HCHO at baseline) Responders showed overall greater postprandial GLP-1 and PYY response (pre and post-training).

Table A-2 continued

Study	Participants	Training intervention	Setting	Outcome measures	Results
Martins et al. (2017)	Obese men and women HIIT: n = 16 (40% men); age = 34±8 years; BMI baseline = 33.2±3.5 kg/m^2; BMI post = NR; body fat = NR; VO_{2max} baseline = 31.1±4.9 mL/kg/min; VO_{2max} post = +2.8±2.6 mL/kg/min ½ HIIT: n=16 (80% men); age = 34±7 years; BMI baseline = 32.4±2.9 kg/m^2; BMI post = NR; body fat = NR; VO_{2max} baseline = 29.6±6.2 mL/kg/min; VO_{2max} post = +4.4±2.2 mL/kg/min Continuous training: n = 14 (60% men); age = 33±10 years; BMI baseline = 33.3±2.4 kg/m^2; BMI post = NR; body fat = NR; VO_{2max} baseline = 31.1±5.3 mL/kg/min; VO_{2max} post = +2.9±2.9 mL/kg/min	12 wk supervised (3d/wk) HIIT (8 s at 85-90% HR_{max} and 12 s recovery for 250 kcal), ½ HIIT (8 s at 85-90% HR_{max} and 12 s recovery for 125 kcal), or continuous exercise (250kcal at 70% of HR_{max}).	Laboratory: Standardized breakfast	Hunger, fullness, PFC and desire to eat (VAS), acylated ghrelin, GLP-1, PYY_{3-36} over 3h post-breakfast Food reward (Leeds Food Preference Questionnaire) before and after breakfast	Increase in fasting and 3-h AUC hunger post-training in all groups. No changes in fasting or postprandial appetite-related hormones or in food reward post-training.

Table A-2 continued

Study	Participants	Training intervention	Setting	Outcome measures	Results
Panissa et al. (2016)	Women HIIT: n = 11; age = 31±15 years; BMI baseline = 25.9±4.1 kg/m^2; BMI post = 25.5±4.2 kg/m^2; body fat baseline = 30.4±6.2 %; body fat post = 27.5±6.2 %; VO_{2max} baseline = 26.5±7.3 mL/kg/min; VO_{2max} post = 34.8±10.5 mL/kg/min MICT: n = 12; age = 26±9 years; BMI baseline = 23.3±2.3 kg/m^2; BMI post = 23.2±2.3 kg/m^2; body fat baseline = 27.7±3.6 %; body fat post = 26.4±3.6 %; VO_{2max} baseline = 31.7±6.2 mL/kg/min; VO_{2max} post = 36.9±7.4 mL/kg/min	6 wk supervised (3d/wk) HIIT (22 min of 1 min at 90% HR_{max} and 30-s recovery at 60% HR_{max}) or MICT (29 min at 70% HR_{max}) with 3 min warm up and cool down at 60% HR_{max}	Free-living	Food intake (3-day food record)	No changes in energy intake after the training interventions.

Table A-2 continued

Study	Participants	Training intervention	Setting	Outcome measures	Results
Rocha et al. (2016)	Men n = 11; age = 26±5 years; BMI baseline = 24.6±3.8 kg/m^2; BMI post = 24.1±3.6 kg/m^2; body fat baseline = 17.4±7.3 %; body fat post = 16.3±7.1 %; VO_{2max} baseline = 43.1±7.4 mL/kg/min, VO_{2max} post = 51.1±8.4 mL/kg/min	12 wk supervised aerobic exercise 3d/wk, up to 4d/wk after 3 wk (5-10min warm-up, 40 min at 50-60% $HR_{reserve}$, 5-10 min cool down)	Free-living	Food intake (7-day food record) Restraint, uncontrolled eating, emotional eating, food cravings	No differences in uncontrolled eating or emotional eating, but trend towards an increase in restraint post-training. Reduction in cravings post-training. No changes in energy or macronutrient intake with training.
Sim et al. (2015) Exercise groups	Overweight men (age = 31±8 years) HIIT: n = 10; BMI baseline = 27.4±1.6 kg/m^2; BMI post = 27.1±1.4 kg/m^2; body fat baseline = 32.0±2.9 %; body fat post = 30.9±2.7 %; VO_{2peak} baseline = 34.8±4.5 mL/kg/min; VO_{2peak} post = 40.4±4.4 mL/kg/min Continuous moderate-intensity training: n = 10; BMI baseline = 27.2±1.5 kg/m^2; BMI post = 27.0±2.3 kg/m^2; body fat baseline = 31.1±5.0 %; body fat post = 30.2±6.5 %; VO_{2peak} baseline = 34.8±6.2 mL/kg/min; VO_{2peak} post = 39.7±6.9 mL/kg/min	12 wk supervised (3d/wk) HIIT (15 s at 170% VO_{2peak} and 60 s at 32% VO_{2peak}) or continuous exercise (60% VO_{2peak}) starting with 30 min and increasing by 5 min every 3 weeks to 45 min.	Laboratory and free-living: LE preload and HE preload	Hunger, fullness, satiation, desire to eat, and PFC (VAS) Food intake (1 test meal after preload and food record for remainder of the day) Glucose, leptin, insulin, AG, PP, and PYY (fasting, and 30 and 60 min post-HEP preload)	Tendency for a reduction in test meal energy intake after HEP post-training in HIIT group only (based on 95% confidence intervals). No change in cumulative energy intake. No change in appetite ratings. Reduction in fasting insulin, insulin sensitivity and leptin (fasting and postprandial) in HIIT group only.

Table A-2 continued

Study	Participants	Training intervention	Setting	Outcome measures	Results
Washburn et al. (2015)	Overweight and obese men and women	10-month supervised walking/jogging (5d/wk with 1 session/wk alternative activities e.g. stationary biking, walking/jogging outside or elliptical) building up to 400kcal/session or 600kcal/session at 70-80% $HR_{max.}$	University cafeteria	Food intake (7 days at baseline, 3.5, 7 and 10 months using digital photography in the cafeteria)	No significant change in absolute energy intake from baseline to post-intervention but energy intake relative to body weight increased in the 600kcal group and was unchanged in the 400kcal group from baseline to 10 months.
Exercise groups	400kcal/session: n = 36; age = 23±3 years; BMI baseline = 31.2±5.6 kg/m^2; BMI post = NR; body fat baseline = 39.6±7.5 %; body fat post = NR; VO_{2max} baseline = 33.4±6.5 mL/kg/min; VO_{2max} post = NR			Diet quality (Healthy Eating Index 2010)	No effect of training on diet quality.
	600kcal/session: n = 37; age = 23±4 years; BMI baseline = 30.6±3.9 kg/m^2; BMI post = NR; body fat baseline = 40.2±6.2 %; body fat post = NR; VO_{2max} baseline = 34.1±5.7 mL/kg/min; VO_{2max} post = NR				

Appendix B

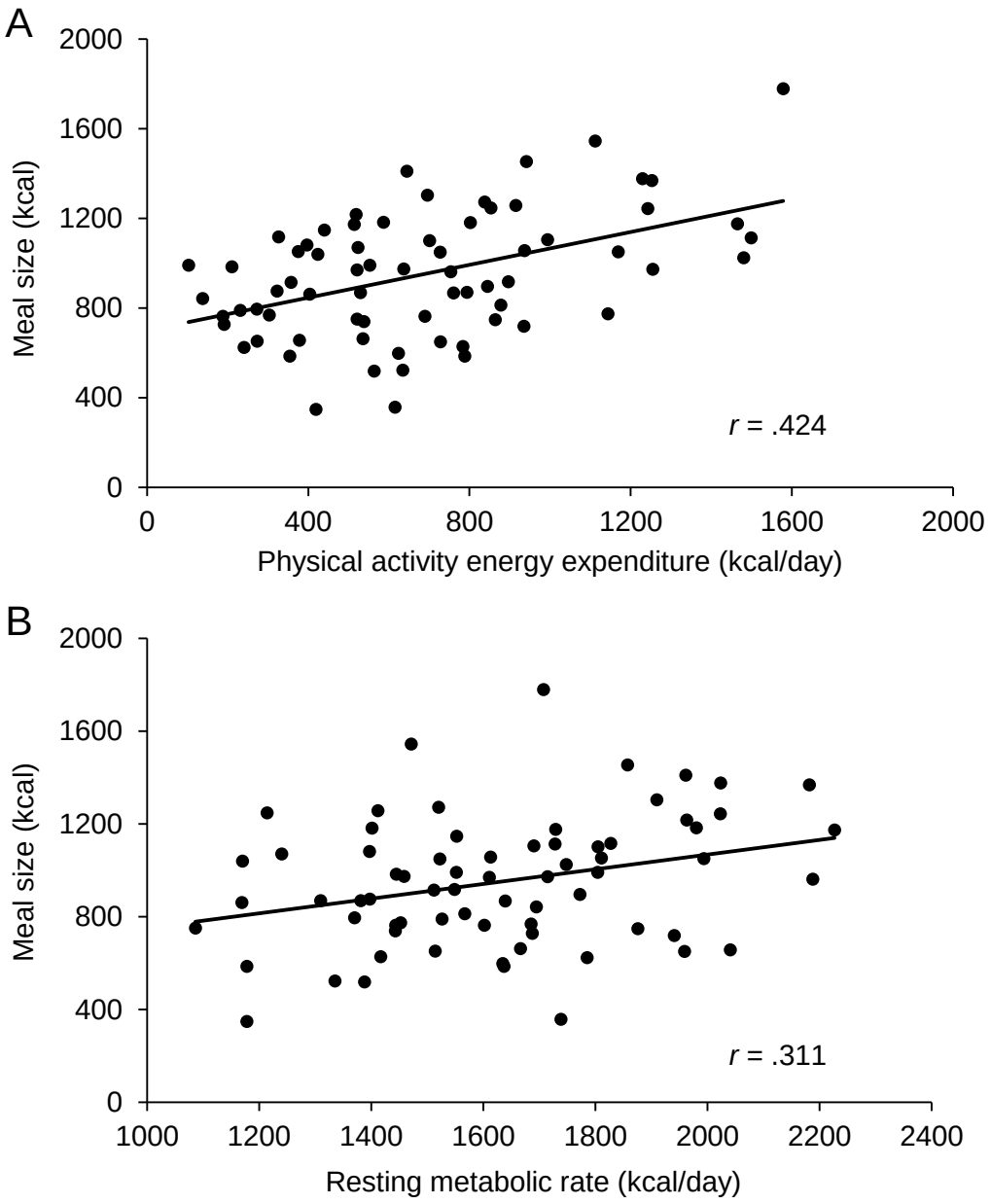

Figure B-1 Scatter plots illustrating the relationship between meal size and physical activity energy expenditure (A) and resting metabolic rate (B)

Appendix C

Table C-1 Participant characteristics before and after the 12-week intervention according to sex-specific median split of body fat loss

	Low body fat loss (*n*=21; 14 females, 7 males)			High body fat loss (*n*=22; 15 females, 7 males)		
	Week 0	**Week 13**	**Change**	**Week 0**	**Week 13**	**Change**
Age (years)	43.1			43.4		
BMI ($kg \bullet m^{-2}$)*†	32.4 ± 4.2	32.4 ± 4.0	0.0	29.2 ± 2.8	28.0 ± 2.8	-1.2**
Total mass (kg)*†	91.5 ± 16.9	91.3 ± 15.9	-0.2	83.1 ± 10.9	79.7 ± 10.4	-3.4**
Body fat (%)*†	42.9 ± 6.9	42.5 ± 6.9	-0.4	38.6 ± 7.1	34.9 ± 7.7	-3.6**
Fat mass (kg)*†	39.3 ± 9.6	38.9 ± 9.5	-0.4	32.0 ± 7.6	27.8 ± 7.2	-4.2**
Fat-free mass (kg)*	52.2 ± 11.2	52.4 ± 10.6	0.3	51.1 ± 8.9	51.9 ± 9.1	0.8**
Waist circumference (cm)*†	105.5 ± 11.8	103.1 ± 11.6	-2.4**	98.2 ± 8.7	93.1 ± 8.1	-5.1**
RMR ($kcal \bullet 24h^{-1}$)	1785.8 ± 325.6†	1735.6 ± 278.7	-50.2	1588.1 ± 278.6	1673.5 ± 243.6	85.4[1]
VO_{2max} ($mL \bullet kg^{-1} \bullet min^{-1}$)*	33.5 ± 8.1	36.6 ± 7.3†	3.1**	32.5 ± 7.5	41.1 ± 5.8	8.6**
Glucose ($mmol \bullet L^{-1}$)[2]	4.8 ± 0.8	4.9 ± 0.8	0.1	5.0 ± 0.9	4.6 ± 1.2	-0.4
Total ghrelin ($pg \bullet mL^{-1}$)[2]	568.8 ± 299.5	546.1 ± 316.6	-22.6	546.6 ± 234.6	668.1 ± 238.1	121.5**
Leptin ($ng \bullet mL^{-1}$)[2]*	48698.2 ± 33482.1	46169.2 ± 37647.3	-2529.0	39509.3 ± 24266.2	25685.9 ± 17820.3	-13823.3**
Insulin ($ng \bullet L^{-1}$)[2]†	1298.9 ± 700.7	1180.2 ± 698.7	-118.7	795.0 ± 241.0	785.4 ± 380.3	-9.6
GLP-1 ($ng \bullet L^{-1}$)[3]	38.1 ± 20.9	44.3 ± 30.6	6.2	24.7 ± 13.2	40.4 ± 33.0	15.7
Total PYY ($ng \bullet L^{-1}$)[4]*	69.2 ± 46.6	93.0 ± 67.5	23.8	52.0 ± 33.1	83.9 ± 57.1	31.9

*Main effect of exercise intervention $p<.05$; †Between group difference $p<.05$; **Within group difference $p<.05$.
[1]Within group difference $p=.06$; [2]Low body fat loss $n=12$, High body fat loss $n=16$; [3]Low body fat loss $n=10$, High body fat loss $n=12$;
[4]Low body fat loss $n=9$, High body fat loss $n=15$