Role of physical activity in regulating appetite and body fat

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Abstract

Recent articles in the press have questioned the role of physical activity in regulating appetite and controlling bodyweight. These articles can be confusing and misleading for the public. Yet this is a complex area and there is disagreement about the importance of physical activity even among academics. Uncertainty and misunderstanding in this area may be related to the heterogeneity of the term 'physical activity' which encompasses sporting pursuits with extremely high levels of energy expenditure over prolonged periods of time, as well as everyday tasks involving much lower levels of energy expenditure on an intermittent basis. This latter form of physical activity includes what has been termed 'non-exercise activity thermogenesis' (NEAT). In the right circumstances, physical activity can make a major contribution to the maintenance of a healthy weight even in the absence of dietary control although a combination of the two is almost certain to be more effective. In the long-term, evidence suggests that for most people exercise is likely to lead to only modest weight loss. This may be due to an insufficient amount of physical activity being performed together with compensatory changes in eating and exercise behaviours. This is hard to prove because energy intake and energy expenditure are difficult to quantify in free-living situations. Individual differences in the way people respond to exercise due to both environmental (*e.g.* social class, education level, income, eating and exercise behaviours of family and peers, weather *etc*.) and genetic factors also contribute to uncertainty about the effectiveness of physical activity for weight control. Nevertheless, physical activity remains a vital component of a healthy lifestyle due to its positive influence on energy balance as well as its potential to reduce the risk of lifestyle-related diseases.

Introduction

Physical activity is widely promoted as a health enhancing behaviour capable of reducing the risk of major diseases including heart disease, stroke, type 2 diabetes, breast cancer and colon cancer (Kyu *et al.* 2016), as well as premature all-cause mortality (Ekelund *et al.* 2016). Physical activity is also promoted for the maintenance of a healthy body composition and for the prevention and management of overweight and obesity (American College of Sports Medicine 2009; World Health Organisation 2016). In this latter respect, efforts have been undermined by a series of articles in the popular press with headlines including 'Why exercise won't make you thin' (*The Times* 2009; *The Guardian* 2010), 'Does running make you fat?' (*The Independent* 2011) and 'Could exercise be making you fat?' (*The Telegraph* 2015). These articles often suggest (whilst providing limited evidence) that exercise stimulates appetite and promotes overconsumption of food. Yet scepticism about the role of exercise in countering weight gain and obesity is not limited to the media and recent articles by leading academics have been categorical in their dismissal of exercise. Malhotra and colleagues (2015), for example, state 'It is time to bust the myth of physical inactivity and obesity: you cannot outrun a bad diet'. Similarly Luke and Cooper (2013) argue 'Physical activity does not influence obesity risk: time to clarify the public health message'. The view of these authors is that overweight and obesity are caused by excess energy intake rather than insufficient energy expenditure and hence efforts to counter the 'obesity pandemic' through physical activity are futile.

The purpose of the present paper is not to debate the relative contributions of diet versus physical inactivity as contributing factors to the obesity pandemic. Rather, this article seeks to provide clarity to the debate about the role of physical activity for weight control and in so doing to increase understanding about both the merits and the limitations of physical activity in this regard. This article aims to complement the excellent articles published in this journal by Professor John Blundell (Blundell 2009; Blundell 2011).

Definition of physical activity and related terms

To appreciate the varied ways in which physical activity can influence energy expenditure, it is important to define what is meant by the term 'physical activity' and also to understand several related concepts. A commonly accepted definition of physical activity is 'any bodily movement produced by contraction of skeletal muscle that substantially increases energy expenditure' (Howley 2001). As a related term, 'exercise' is defined as 'a subcategory of leisure-time physical activity in which planned, structured and repetitive bodily movements are performed to improve or maintain one or more components of physical fitness' (Howley 2001). In recent years, two additional concepts have emerged which are important for any discussion of the relationship between physical activity and weight regulation; these are 'sedentary'/'sedentary behaviour' and 'non-exercise activity thermogenesis' (NEAT). Sedentary behaviour may be defined as '… any waking behaviour characterised by an energy expenditure ≤1.5 METs while in a sitting or reclining posture' (Sedentary Behaviour Research Network 2012). A MET (metabolic equivalent of task) is the energy expenditure at rest, so sedentary behaviour is defined as behaviour involving sitting or lying down and at the same time expending energy at a very low rate (*i.e.* ≤1.5 METs). Light-intensity activities are defined as requiring 1.6–2.9 METs, moderate-intensity activities 3.0–5.9 METs and vigorous-intensity activities ≥6 METs (Ainsworth *et al.* 2011; Pate *et al.* 2008). The Sedentary Behaviour Research Network (2012) recommends the term 'inactive' to describe individuals '… who are performing insufficient amounts of moderate- to vigorous-intensity physical activity (*i.e.* not meeting specified physical activity guidelines)'. In this regard, NEAT becomes important. NEAT '… is the energy expended for everything we do that is not sleeping, eating or sports-like exercise. It ranges from the energy expended walking to work, typing, performing yard work, undertaking agricultural tasks and fidgeting' (Levine 2002). Thus, there is overlap between the terms physical activity and NEAT, but

NEAT also captures the energy expenditure from movements which may be classed as inactive but not sedentary according to the Sedentary Behaviour Research Network (2012). This is important because the energy expenditure due to NEAT may be a significant factor in preventing overweight and obesity and the diseases associated with these conditions (Hamilton *et al.* 2007).

Are low levels of physical activity associated with weight gain and obesity?

Many studies have demonstrated an association between low levels of physical activity (and/or high levels of sedentary behaviour) and the risk of overweight and obesity. These studies have used a variety of methods to assess physical activity/sedentary behaviour including questionnaires (Hancox *et al.* 2004), inclinometers and accelerometers (Levine *et al.* 2005; Shook *et al.* 2015) and doubly labelled water (Esparza *et al.* 2000). Such studies consistently demonstrate an association between low levels of physical activity/high levels of sedentary behaviour (*e.g.* TV viewing) and the risk of weight gain/obesity. The study by Levine and colleagues (2005) is particularly interesting because it observed much higher levels of NEAT in a group of lean individuals than in a group of obese individuals, despite both groups describing themselves as 'couch potatoes'. This demonstrates the complexity of the issue. If questionnaires had been used to assess physical activity habits, presumably both groups studied by Levine and colleagues would have been classed as inactive. However, by assessing body posture and movement every half a second for 10 days in all participants Levine and colleagues were able to detect that lean individuals expended approximately 350 kcal/day more than their obese counterparts due to NEAT (Fig. 1). Levine and colleagues estimated that if the obese individuals in their study adopted the 'NEAT enhanced behaviour' of their lean counterparts for a year they might lose 15 kg in weight assuming energy intake remained unchanged (an issue discussed below). Although these studies provide clear evidence of a link between physical inactivity and risk of obesity, they are observational studies and are not proof of cause and effect. One possible explanation for these findings is that they represent reverse causation (*i.e.* as people become overweight and obese they become less active). Moreover, Hankinson and colleagues (2010) observed that even when people maintain very high levels of physical activity over decades weight gain still occurs albeit to a lesser extent than in individuals who are less active (Fig. 2). This finding has been supported in a more recent study whereby men and women classified in the lowest quintile of physical activity experienced the greatest increase in fat mass after 12 months of observation. However, a significant, albeit smaller, increase in fat mass was still observed after 12 months in those in the highest physical activity quintile (Shook *et al.* 2015).

INSERT FIGURE 1 HERE

INSERT FIGURE 2 HERE

Does increased physical activity lead to weight loss?

Well-controlled intervention studies demonstrate conclusively that increased physical activity, either alone or in combination with dietary restriction, can lead to substantial weight loss. The work of John Jakicic and colleagues provides a notable example. In one study conducted over 12 months, a combination of exercise (energy expenditure: 1000 - 2000 kcal/week) and dietary restriction (energy intake: 1200 - 1500 kcal/day) caused significant weight loss in previously inactive women and a dose-response relationship was observed between the amount of physical activity performed and the amount of weight lost (Jakicic *et al.* 2003). Follow-up of these same individuals at 24 months revealed that those who maintained high levels of physical activity (an average of 1835 kcal/week; 275 min/week) together with dietary restriction were able to sustain a weight loss of more than 10% (Jakicic *et al.* 2008). Another notable study is that conducted by Robert Ross and colleagues (2000a). This study examined the effects of diet versus exercise for weight loss in 52 obese men over a 12-

week period. A diet only group were asked to reduce their food intake by 700 kcal/day over the 12-week intervention period, whereas an exercise only group were asked to keep dietary intake constant but increase their physical activity levels by 700 kcal/day over the 12 weeks. The findings revealed an average weight loss of 7.5 kg in both groups, with a greater fat loss in the exercise group than the diet group (Fig. 3). The authors concluded that 'weight loss induced by increased daily physical activity without caloric restriction substantially reduces obesity (particularly abdominal obesity) … and prevents further weight gain' (Ross *et al.* 2000a). A review paper comparing diet only with exercise only interventions for weight loss confirmed that exercise without dietary restriction is an effective strategy for reducing obesity and related co-morbidities (Ross *et al.* 2000b). Although these studies clearly demonstrate that physical activity can result in substantial weight loss, a meta-analysis of randomised, controlled trials concluded that exercise alone generally results in modest (<5 kg) weight loss (Shaw *et al.* 2006). This provokes the question of what factor or factors might be responsible for the modest weight loss often seen with exercise and whether there is a compensatory increase in food intake which counters exercise-induced weight loss.

INSERT FIGURE 3 HERE

Does physical activity increase appetite and food intake?

Studies attempting to answer this question fall into two broad categories: those examining single bouts of exercise (acute responses) and those examining exercise training performed over a period of weeks or months (chronic responses). Many studies have examined appetite, appetite hormone and energy intake responses to acute bouts of exercise, and the general consensus is that in the short-term (over the course of a day or two) there is not a strong relationship between energy expenditure and energy intake (Blundell *et al.* 2003; Donnelly *et al.* 2014). This has been demonstrated for a variety of activities including walking (King *et al.* 2010), running (Alajmi *et al.* 2016; Douglas et al 2015; King *et al.* 2011a), swimming (King *et al.* 2011b) and cycling (Deighton *et al.* 2013a; Deighton *et al.* 2013b). Of particular note are studies which have directly compared energy deficits created via diet or exercise. These studies demonstrate that there are compensatory changes in appetite perceptions, appetite hormones (ghrelin and peptide YY) and food intake in response to dietary-induced energy deficits but not exercise-induced energy deficits in both women (Alajmi *et al.* 2016) and men (King *et al.* 2011a) (Fig. 4).

INSERT FIGURE 4 HERE

Whether physical activity/exercise increases energy intake in the longer term is less certain due to the difficulty of objectively measuring energy intake in free-living conditions. A recent systematic review concluded that there was no consistent evidence that increased physical activity or exercise affects energy or macronutrient intake but the authors of this review acknowledged that there are limitations to the existing literature, including a lack of adequately powered trials and objective monitoring of energy expenditure and energy intake (Donnelly *et al.* 2014).Intuitively, one would expect energy intake to increase at some stage in response to a chronic period of physical activity/exercise training and John Blundell and colleagues (2003) concluded in their review paper that there is partial but incomplete compensation (perhaps accounting for about 30% of the energy expended) in the weeks after an increase in physical activity. In contrast, another recent systematic review concluded that 'energy compensation' approached 84% of energy expended for long-term (about 80 weeks) exercise interventions but few studies were conducted over this length of time and the review was not able to establish whether this compensation was due to increased energy intake, decreased energy expenditure or a combination of the two (Riou *et al.* 2015). Thus, there remains considerable uncertainty in this area.

The factors underlying compensatory increases in appetite and food intake in response to chronic periods of increased physical activity/exercise training have not been well studied. Weight loss appears to be a major driver for eliciting compensatory responses – at least in the case of studies involving dietary intervention. In one study involving 50 overweight and obese men and women consuming a very low-energy diet over a period of 10 weeks, an average weight loss of 13.5 kg was observed. One year later the participants had gained some weight but an average weight loss of 7.9 kg (compared with baseline weight) was still evident. The authors quantified subjective appetite ratings and appetite-regulatory hormone concentrations in response to a standardised meal before and after the dietary intervention and they observed significant elevations in ghrelin and perceived hunger and significant reductions in mean levels of peptide YY, cholecystokinin and insulin in response to this meal. Fasting leptin levels were also reduced after weight loss in this study (Sumithran *et al.* 2011). Although hormonal changes have not always been found to predict weight regain after weight loss (Strohacker *et al.* 2014), such 'physiological adaptations' are thought to favour weight regain suggesting it is difficult to 'overcome physiology with behaviour' (Greenway 2015). Evidence relating to compensatory changes in hormones and appetite perceptions after periods of exercise training is very limited, but there is some evidence that physical activity may improve the sensitivity of the appetite control system in such a way as to enhance satiety and facilitate weight loss maintenance (Beaulieu *et al.* 2016; Lean and Malkova 2016; Stensel 2010).

In contrast to situations when energy expenditure is increased, it appears that reductions in energy expenditure provide a significant challenge to energy balance and increase the chances of weight gain. In a well-controlled experiment conducted by James Stubbs and colleagues (2004), six young men spent two, week-long periods in a whole body indirect calorimeter. In one of these periods the men remained sedentary (1.4 x resting metabolic rate) while in the other period they were moderately active (1.8 x resting metabolic rate). During both periods the men had free access to food, and energy intake was continually monitored. Cumulative energy balance was 26.3 MJ in the sedentary trial and 11.1 MJ in the moderately active trial. The investigators concluded that the enforcement of a sedentary routine does not induce a compensatory reduction of energy intake. The implications are that a sedentary lifestyle facilitates fat storage and weight gain (Stubbs *et al.* 2004).

Do increases in physical activity lead to compensatory reductions in non-exercise activity thermogenesis?

Aside from the possibility that increases in physical activity may increase energy intake to some degree, there is also the possibility that increases in planned physical activity/structured exercise will be countered by subconscious reductions in energy expenditure in unstructured physical activity (*i.e*. NEAT). The study of Levine and colleagues (2005) mentioned earlier demonstrates that NEAT alone can account for substantial differences in energy expenditure between individuals. If NEAT is subconsciously reduced in response to an exercise training intervention, clearly this could reduce or even nullify any weight loss. A review of this topic encompassing 31 research articles found minimal evidence to support the hypothesis that prescribed physical activity/exercise training results in decreased NEAT, but the authors highlighted that there is a lack of data from adequately powered trials using objective measurements (Washburn *et al.* 2013). A more recent review and meta-analysis using a mathematical modelling approach concluded that there is 'substantial' compensation in both dietary and exercise interventions for weight loss (Dhurandhar *et al.* 2015). The extent to which this compensation is due to changes in NEAT is unclear. The review highlighted that there may be a range of behavioural and metabolic compensations that can be very difficult to quantify but which may reduce the expected amount of weight loss following a given intervention. Importantly, small but persistent average daily imbalances between energy intake and expenditure (perhaps as small as 30 kJ per day) are sufficient to alter bodyweight (Hall *et al.* 2011; Speakman *et al.* 2011) and current methods of assessing energy intake and expenditure in free-living situations

are not accurate enough to detect such an imbalance. Currently, there is insufficient evidence to definitively answer the question of whether increases in physical activity lead to compensatory reductions in NEAT, but it is feasible that some compensation may occur. Related to this issue is the concept of constrained total energy expenditure proposed by Herman Pontzer (Pontzer 2015; Pontzer *et al.* 2016). Pontzer hypothesises that total energy expenditure is relatively stable and is regulated homeostatically, such that total daily energy expenditure does not increase in proportion to physical activity in an additive way. Rather, total energy expenditure is constrained within a narrow range such that metabolic activity (*e.g.* NEAT) is reduced when physical activity is increased. Pontzer suggests that this has an evolutionary advantage favouring survival. Although there are limitations to this model (Ravussin & Peterson 2015), it does highlight another factor which may help explain why weight loss may be lower than expected with an exercise intervention.

Why are some individuals more responsive to exercise than others?

Another factor to consider in relation to physical activity and weight loss is that individual responses are likely to be highly variable (Blundell 2011; Hopkins *et al.* 2010; King *et al.* 2008). This may be due to both biological/metabolic variability (*e.g.* differences in the economy of movement and hence energy expenditure) and also to behavioural variability (differences in the extent of compensatory eating and physical activity/NEAT levels). These factors in turn may be influenced by both environmental and genetic factors. Regarding the former, there are a host of environmental factors which may influence eating and exercise behaviours including social class, education level, income, eating and exercise behaviours of family and peers and ambient conditions (*e.g.* temperature, weather, altitude). With respect to the latter, a study involving identical twins demonstrated wide variations in weight loss with a programme of cycling exercise (Bouchard *et al.* 1994). In this study, the weight loss responses were more similar within twin pairs than between twin pairs suggesting some degree of genetic influence. This was particularly true with reductions in visceral fat. This raises the question of which genes are involved and how these genes are operating to influence weight loss. This is an area of ongoing research. Many genes are likely to play a role and each gene may operate by a different mechanism. The most extensively studied gene linked to obesity in the general population is the fat mass and obesity associated (FTA) gene which was first identified by Frayling and colleagues (2007). They showed that those who were homozygous for the risk allele (*i.e.* AA individuals – about 16% of the UK/European populations studied) weighed about 3 kg more and had a 1.7 fold higher risk of obesity than those who had not inherited a risk allele (*i.e.* TT individuals). It has been shown since that the FTO gene exerts its effect on body mass by regulating the appetite hormone ghrelin, predisposing those with the FTO risk variant to increased energy intake and obesity (Karra *et al.* 2013). Importantly, the findings of a recent meta-analysis suggest that lifestyle interventions are likely to induce greater weight loss in those with the risk allele (AA and AT individuals) than in those without it (TT individuals) (Xiang *et al.* 2016). Physical activity may also interact positively with multiple genes as demonstrated by Li and colleagues (2010). They calculated a genetic predisposition score from 12 single nucleotide polymorphisms in obesity-susceptibility loci and observed a lower body mass index in those classified as active compared with those classified as inactive, even when participants were matched for genetic susceptibility (Fig. 5). This suggests that physical activity can modify genetic predisposition to weight gain and obesity. Genetic factors in turn are likely to explain in part why some individuals experience greater weight loss with exercise than others.

INSERT FIGURE 5 HERE

Summary and conclusions

Physical activity is a broad term encompassing various means of expending energy from formal/structured exercise to everyday activities including walking, climbing stairs and domestic tasks resulting in NEAT. Higher levels of physical activity (including NEAT) are associated with lower body mass index and percentage body fat values and for those who are overweight and obese increased physical activity levels can be effective for lowering body mass and body fatness. In the long-term, weight loss from physical activity is often less than expected and this may be due to a lack of compliance to exercise programmes and/or compensatory responses in energy intake and energy expenditure. These are difficult to monitor and quantify in free-living situations and hence difficult to predict. There are also individual differences in weight loss responses to exercise. These may be partly explained by compensatory changes in eating and exercise behaviours and are exacerbated by genetic factors. Assertions such as 'physical activity does not influence obesity risk' (Luke and Cooper 2013) are an overstatement based on the evidence but a cursory examination of the calories contained in foods and the energy expenditure resulting from physical activity reveals that it is easy to compensate for the calories expended in exercise without some dietary vigilance. In this sense, for most people, there is some truth in the statement 'you cannot outrun a bad diet' (Malhotra *et al.* 2015).

Regardless of whether obese individuals are attempting to lose weight via diet, physical activity or a combination of the two, the odds of success are not good. A recent UK primary care study observed that even for 'simple obesity' (body mass index = 30 - 34.9 $kg \cdot m^{-2}$) the annual probability of attaining normal weight is 1 in 210 for men and 1 in 124 for women (Fildes *et al.* 2015). Nevertheless, The National Weight Control Registry in the US demonstrates that there are individuals who are highly successful at losing weight and maintaining weight loss and the key characteristics of such individuals are a combination of dietary restraint and high levels of physical activity (Klem *et al.* 1997). Thus, physical activity can make a valuable contribution to energy balance and weight control and it should continue to be promoted for this and the many other health benefits it confers (Hardman and Stensel 2009).

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Figure legends

Figure 1 Time spent lying, sitting, and standing and ambulating in 10 obese and 10 lean sedentary subjects. Note that the lean individuals spent significantly less time sitting and significantly more time standing and ambulating than the obese individuals (as indicated by the asterisks). Values are mean (SEM). Adapted from Levine *et al*. (2005) with permission.

Figure 2 Unadjusted body mass index (BMI) over time in men and women according to habitual physical activity level (low, moderate or high) in the Coronary Artery Risk Development in Young Adults (CARDIA) study. Note that BMI gain was lowest in the highest activity group but even in this group BMI gain occurred. Values are means. Figure based on data from Hankinson *et al.* (2010).

Figure 3 Change in body weight and fat distribution after 3 months in diet-only and exercise-only weight loss intervention groups. Note that both interventions were effective but the exercise-only intervention led to a greater loss of total fat (as indicated by the asterisk). Values are mean (SD). Adapted from Ross *et al*. (2000a) with permission.

Figure 4 Total area under the curve for acylated ghrelin and PYY_{3-36} in men (n = 12) and women (n = 11) in control (energy balance), exercise deficit and food deficit conditions. Note that ghrelin (a hunger hormone) is increased and PYY_{3-36} (a hunger suppressing hormone) is decreased under food deficit conditions while the opposite occurs under exercise deficit conditions (as indicated by the asterisks). Values are mean (SEM). Data for men adapted from King *et al.* (2011a) and data for women adapted from Alajmi *et al.* (2016) with permission.

Figure 5 Body mass index (BMI) values in low (≤ 11 BMI-increasing risk alleles) and high (> 11 BMI-increasing risk alleles) genetic susceptibility groups identified in the EPIC-Norfolk Prospective Population Study. Note that physical activity counters the effects of genetic susceptibility as indicated by a significant interaction effect. Values are mean (95% confidence intervals). Adapted from Li *et al.* (2010) with permission.

Figure 1

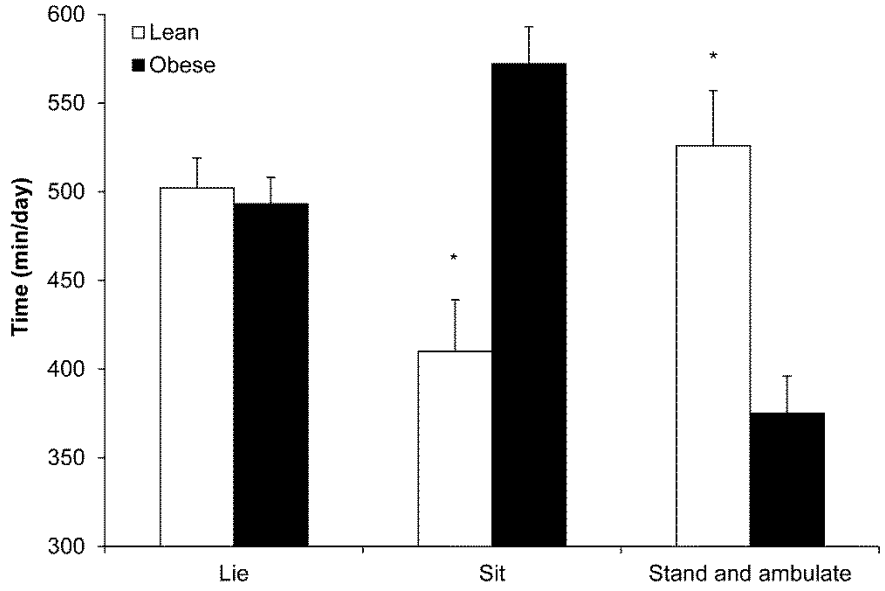

600
550
500
450
400
350
300
Time (min/day)
Lean
Obese
*
*
Lie
Sit
Stand and ambulate

Figure 2

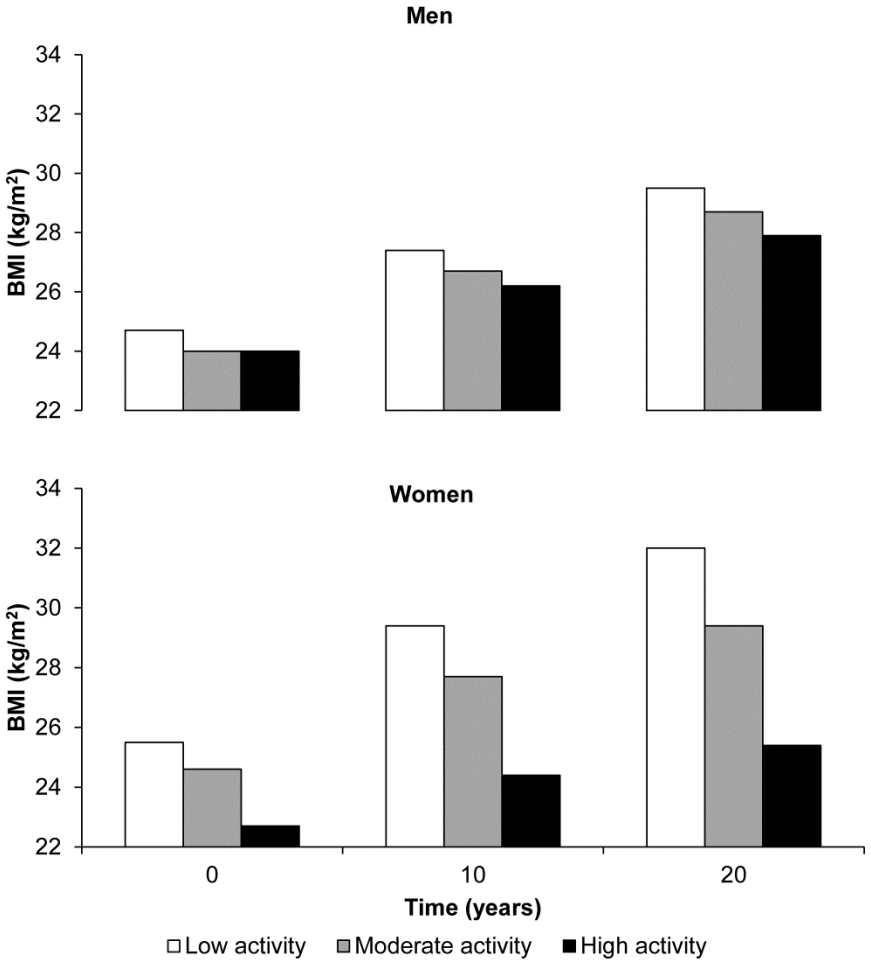

Men
34
32
30
28
26
24
22
BMI (kg/m2)
Women
34
32
30
28
26
24
22
BMI (kg/m2)
0
10
20
Time (years)
Low activity
Moderate activity
High activity

Figure 3

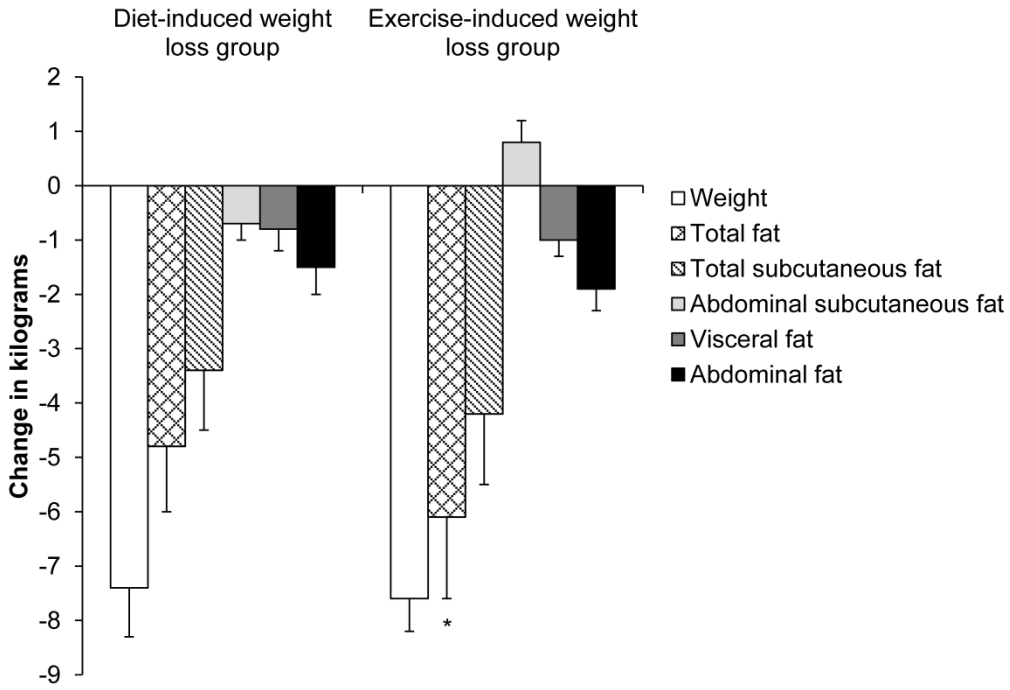

Diet-induced weight loss group
Exercise-induced weight loss group
Change in kilograms
2
1
0
-1
-2
-3
-4
-5
-6
-7
-8
-9
*
Weight
Total fat
Total subcutaneous fat
Abdominal subcutaneous fat
Visceral fat
Abdominal fat

Figure 4

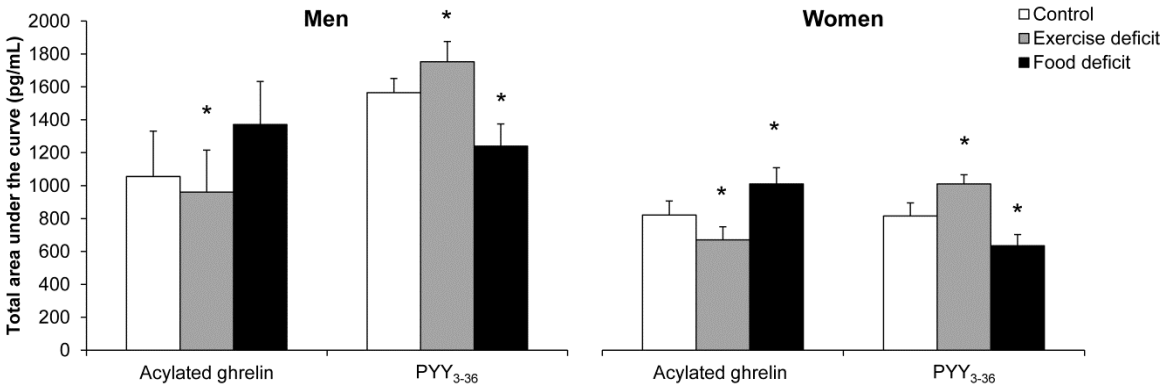
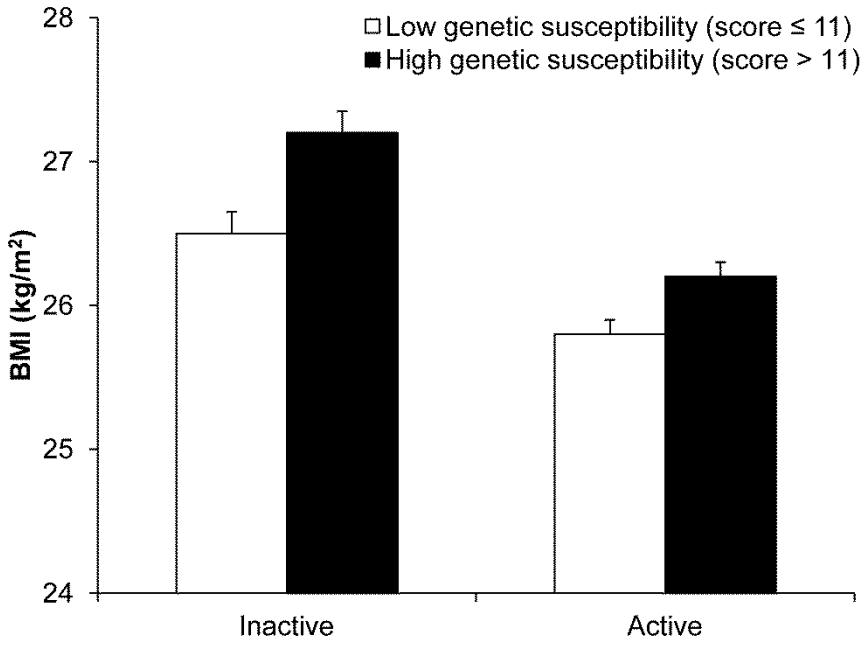

Men
Women
Control
Exercise deficit
Food deficit
Total area under the curve (pg/mL)
2000
1800
1600
1400
1200
1000
800
600
400
200
0
*
Acylated ghrelin
PYY3-36

Figure 5


Low genetic susceptibility (score ≤ 11)
High genetic susceptibility (score > 11)
BMI (kg/m²)
28
27
26
25
24
Inactive
Active