Review

Appetite control and energy balance: impact of exercise

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Summary

Exercise is widely regarded as one of the most valuable components of behaviour that can influence body weight and therefore help in the prevention and management of obesity. Indeed, long-term controlled trials show a clear dose-related effect of exercise on body weight. However, there is a suspicion, particularly fuelled by media reports, that exercise serves to increase hunger and drive up food intake thereby nullifying the energy expended through activity. Not everyone performing regular exercise will lose weight and several investigations have demonstrated a huge individual variability in the response to exercise regimes. What accounts for this heterogeneous response? First, exercise (or physical activity) through the expenditure of energy will influence the energy balance equation with the potential to generate an energy deficit. However, energy expenditure also influences the control of appetite (i.e. the physiological and psychological regulatory processes underpinning feeding) and energy intake. This dynamic interaction means that the prediction of a resultant shift in energy balance, and therefore weight change, will be complicated. In changing energy intake, exercise will impact on the biological mechanisms controlling appetite. It is becoming recognized that the major influences on the expression of appetite arise from fat-free mass and fat mass, resting metabolic rate, gastric adjustment to ingested food, changes in episodic peptides including insulin, ghrelin, cholecystokinin, glucagon-like peptide-1 and tyrosine-tyrosine, as well as tonic peptides such as leptin. Moreover, there is evidence that exercise will influence all of these components that, in turn, will influence the drive to eat through the modulation of hunger (a conscious sensation reflecting a mental urge to eat) and adjustments in postprandial satiety via an interaction with food composition. The specific actions of exercise on each physiological component will vary in strength from person to person (according to individual physiological characteristics) and with the intensity and duration of exercise. Therefore, individual responses to exercise will be highly variable and difficult to predict.

Keywords: Appetite, body composition, energy balance, energy intake.

In the surveys so far carried out the time spent sitting has varied from 8¾ to 10¾ h/day and the time lying down has been of the same order. It looks as though man should be regarded now, if not in the past, as a predominantly sedentary rather than an upright animal.

—Edholm, Fletcher, Widdowson and McCance (1)

Introduction

For a number of reasons – both theoretical and practical – it is important to clarify the effect of exercise (physical activity, PA) on energy intake (EI, appetite control). The issue can be approached by addressing two specific questions formulated in classical investigations in the field. First, Edholm *et al.* (1,2) sought to establish a fundamental relationship between energy expenditure (EE) and EI. Behind this was 'the desire to find out more about the mechanisms which relate intake to expenditure – what regulates appetite, in fact' (1). In time-consuming studies on army cadets, measures of energy expended in daily activities and energy consumed in meals and snacks showed no meaningful association within a single day. However, over a 2-week period, there was a clear association between EI and EE. Edholm *et al.* (1) argued that 'the differences between the intakes of food must originate in the differences in energy expenditure'. Strangely, this view was ignored and the general approach to the issue was largely abandoned. Indeed, the strategy of integrative physiology was replaced with molecular biochemistry as a form of enquiry into biology and behaviour. However, just because Edholm's views have been overlooked, does not mean that they were wrong.

A second approach arose from the work of Jean Mayer and especially from his painstaking studies on jute mill workers in Bengal (3). In this Herculean study, a comparison was made between, on one side the physical exertion and effort required by particular forms of work and, on the other side the calculated dietary intake of individual workers. Jobs ranged from heavy-duty tasks such as lifting and sorting to clerical duties and administrative desk jobs requiring little physical effort. It was assumed that the energy expended was closely related to the physical effort of the daily work. In a classic figure from the published study (see top panel Fig. 1), an inverted U-shaped function described the relationship between EE and EI. Interestingly, the right hand portion of the curve showed an approximately linear relationship between EI and EE but only above a certain level of energy EE. This was consistent with the approach demonstrated by Edholm *et al.* (1,2). Indeed, Mayer *et al.* (3) proposed that 'the regulation of food intake functions with such flexibility that an increase in energy output due to exercise is automatically followed by an equivalent increase in caloric intake'. However, Mayer *et al.* (3) also demonstrated that at very low levels of EE – and in work that could be regarded as sedentary – the association between EE and EI was lost and dietary intake increased disproportionately in relation to the energy expended. In this 'sedentary zone' restraint over appetite appeared to be lost. This observation appears to have considerable implications for our current sedentary lifestyles and levels of obesity.
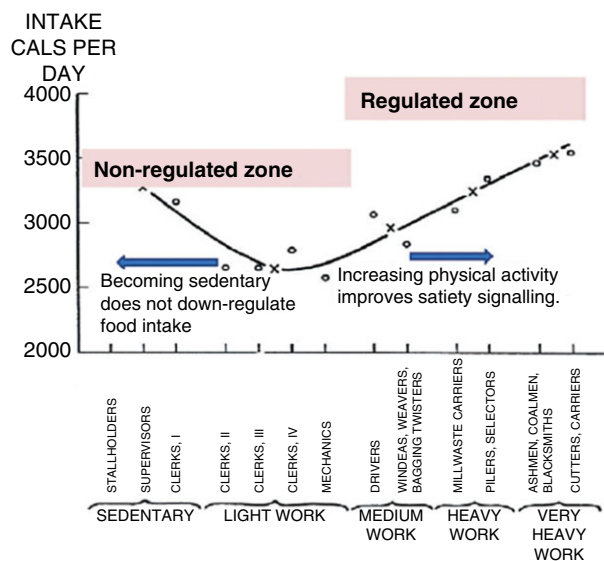

Figure 1 A modified version of the original graphic from the article by Mayer *et al.* (63) on the Bengal jute mill workers showing the relationship between energy expended (according to the physical demands of work) and dietary intake. It is proposed that appetite control is homeostatically regulated when energy expenditure is high but becomes dys-regulated in the sedentary 'non-regulated' zone in which homeostatic control over appetite is weak thereby permitting overconsumption (64).

Interestingly, this picture has been translated into formal terms by Henry Taylor, who related the homeostatic control of appetite to the PA performed.

> . . . the late Henry Taylor favoured a model that linked energy intake to expenditure in a J-shaped curve (personal communication, late 1970s). The first part of his concept was that energy intake was in exact homeostasis with energy expenditure under conditions of high energy expenditure. The second part was that there is a failure of homeostasis in sedentary lifestyles because of its accompanying low energy expenditure. He postulated that bodily 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. (cited by Jacobs (4), p. 1234).

Common perspectives

Currently, there appears to be considerable ambiguity concerning the usefulness of PA for weight loss and this questions its value for dealing with the high prevalence of obesity. On one hand, the public health authorities advise citizens to increase PA levels and to decrease sedentary time (in addition to restraining dietary intake). On the other hand, in recent years, the media has promulgated messages

such as 'Exercise will not make you thin' (Time Magazine), 'Exercise makes you fat' (Daily Telegraph, UK) and 'Why running makes you fat' (Observer, UK). Given these strident claims, it would be surprising if citizens were not confused. Because many people are pleased to read messages about the futility of exercise to reinforce a preference to avoid PA, the implication of this publicity is serious. Importantly, these messages portrayed in the popular media are false. There is clear evidence from large-scale controlled trials that PA carried out over long periods of time produces a dose-dependent reduction in body weight (5,6). The effect is clearly present whether the exercise is measured in minutes of activity per week or in kcal energy expended. On the average, the more exercise carried out, the greater the weight loss. This evidence is supported by the results of a series of reviews (7–9), including a Cochrane Review (the gold standard in assessing evidence) by Shaw *et al.* which concluded that 'exercise has a positive effect on body weight and cardiovascular risk factors in people with overweight and obesity, particularly when combined with a diet' (10). A further systematic review concluded that 'for people starting an exercise programme, this leads to a negative energy balance and a remarkably consistent loss of body fat in relation to the net cost of exercise training' (11). Furthermore, it is well established that the health benefits of regular exercise are independent of any changes in body weight (12).

While such findings indicate that exercise can have a positive effect on body weight (if sufficient energy is expended), these reviews do not directly address Mayer's original question of whether increases in EE automatically result in compensatory increases in EI. The fact that weight loss is seen with regular aerobic exercise suggests that any 'energy-saving' mechanisms do not completely nullify the effects of exercise. Nevertheless, in many cases, the degree of weight lost is somewhat less than that theoretically predicted on the basis of the measured EE and its presumed relationship to tissue lost (13,14). But note that the prediction of weight loss based on such methods has recently been revised (15,16). Moreover, the changes in weight alone do not reveal the mechanisms involved, nor do they identify the physiological processes that produce the changes in body weight. The answer to these issues requires that studies on appetite control are carried out simultaneously with measures of EE. For many years, the study of appetite control and the study of PA have been conducted quite independently – in separate specialized appetite or exercise laboratories – and the changes in EI and EE observed were interpreted in isolation. More recently, appetite research has been embraced within an energy balance framework (17–19). This has lead to the possibility of interpreting the effects of exercise in relation to theories of appetite control and to a phenomenon called 'energy homeostasis'.

The adipocentric model of appetite and energy homeostasis

The theoretical basis for a potential role of exercise in appetite control has never been formulated. Therefore, in seeking to reveal its role, it is useful to have in mind prevailing views that have established the current dogma. Two notions seem to dominate the field; the first of these is the adipocentric concept of appetite control i.e. the view that adipose tissue is the main driver of food intake, with day-to-day food intake controlled in the interests of regulating body weight (and specifically, adipose tissue). During the 1950s, three basic ideas monopolized approaches to 'body weight regulation'; these were the glucostatic (20), aminostatic (21) and lipostatic hypotheses (22). These simple ideas exerted a mild but pervasive influence on thinking about a complex problem. The discovery of leptin in 1994 by Zhang *et al.* (23) seemed to provide conclusive proof of the authenticity of the lipostatic hypothesis (which was based on interpretations of the classic rat studies of Kennedy (22)) and leptin was construed as 'the lipostatic signal' that was an essential component required in a negative feedback process for the regulation of adipose tissue. This idea has been incorporated into models of appetite control in which leptin is depicted as the major signal (the missing link) that informs the brain about the state of the body's energy stores (24,25). In turn, a forceful interpretation of this view has positioned adipose tissue at the centre of appetite control. Indeed, it has been stated by Woods and Ramsay (26) that 'There is compelling evidence that total body fat is regulated . . . when it is decreased reflexes restore it to normal . . . when it is increased reflexes . . . elicit weight loss. These processes account for the relatively stable maintenance of body weight over long periods' and that 'food intake is an effector or response mechanism that can be recruited or turned off in the regulation of body fat'. This view has been incorporated into general thinking about the control of appetite and appears to have been widely accepted. In addition, leptin is understood to play a key role in the control of appetite by adipose tisssue. Although it is beyond doubt that leptin exerts a critical influence in many biochemical pathways concerning physiological regulation (27,28), it has been argued that the role of leptin in the aetiology of obesity is confined to very rare situations in which there is an absence of a leptin signal (29). Others have also argued that the role of leptin signalling is mainly involved in the maintenance of adequate energy stores for survival during periods of energy deficit (30). This is why leptin may be critical in the resistance to weight loss with dieting. More importantly for this article, there is little evidence for a role for leptin in day-to-day appetite control. In addition, the impact of adipose tissue itself has not been shown to exert an influence over the

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parameters of hunger and meal size which are key elements in day-to-day control of appetite.

The second issue that appears to influence thinking is the notion called 'energy homeostasis'. This idea has been proposed to account for the accuracy in which energy balance is maintained over time in normal individuals. A recent commentary has argued that 'for a healthy adult weighing 75 kg typically consuming approximately one million kcal each year, then a mismatch of just 1% (expending 27 kcal per day fewer than consumed) will yield a body fat increase of 1.1 kg after 1 year' (31). This type of calculation which uses the 1 kg of fat for 8,000 kcal rule has recently been shown by Hall *et al.* (15) and others (16) to be simplistic and to produce implausible predictions. Further support, however, has used a study on 15,624 healthy Swedish women that indicated for this cohort an average annual weight gain of 0.33 kg year^{-1} suggesting that for these participants there was an accuracy of >99.5% in the matching of EI to EE (32). Of course, if you only measure humans who remain stable, then you will inevitably find stability. It might be observed in passing that the prevalence of obesity in Sweden is approximately 9% whereas in the United States it is >30%. The relative stability of body weight in Sweden appears to be cultural rather than biological.

Moreover, given the worldwide epidemic of obesity and the apparent ease with which humans appear to gain weight, it seems implausible that some privileged physiological mechanism is regulating body weight with exquisite precision. If such a mechanism existed, it would surely operate to correct weight gain once it began to occur. The compelling phenomenon of dietary-induced obesity (DIO) in rats also suggests that physiology can be overcome by a 'weight-inducing' nutritional environment and that 'energy homeostasis' cannot prevent this. The phenomenon of DIO in rats questions the notion of an all powerful biological regulatory system. Moreover, this experimental 'fact' strongly resonates with the proposal of a human 'obesogenic environment' that promotes weight gain in almost every technologically advanced country on the planet (33). The analogy with DIO in rats is quite compelling and is usually not denied.

However, the existence of energy homeostasis is frequently invoked to account for the readiness of obese people who have lost weight to regain it. But there is no compelling argument why the cause of weight regain in obese people who have slimmed down should necessarily be attributed to the force of a biological imperative (although physiological processes certainly contribute), any more that a biological imperative was responsible for people getting fat in the first place (or for DIO rats getting fat on a high-fat diet). People who have lost weight continue to live in the same obesogenic environment that contributed to their original weight gain. However, the notion of energy homeostasis suggests that there is some 'deus ex machina' whose job is to calculate the total energy transactions in the body and to moderate these to bring about a control of body weight. Moreover, the argument is circular. To the question, why is body weight stable, the answer is because of energy homeostasis. But to the question, what is the evidence for energy homeostasis, the answer is the stability of body weight. Crucially, the case for the operation of energy homeostasis rests on the existence of body weight regulation and stability.

The argument for body weight stability is not compelling. The existence of worldwide obesity suggests that body weight is not tightly regulated. An alternative view that has been discussed for decades is that regulation is asymmetrical (34). While the reduction in body weight is strongly defended, physiology does not resist an increase in fat mass (FM) (35). Indeed, the physiological system appears to permit fat deposition when nutritional conditions are favourable (such as exposure to a high energy-dense diet). This means that the role of culture in determining food selection is critical. In many societies, the prevailing indeology of consumerism encourages overconsumption. This applies not only to foods but to all varieties of material goods. The body is not well protected from the behavioural habit of overconsuming food; processes of satiety can be overridden to allow the development of a positive energy balance. This has been referred to as 'passive overconsumption' (36,37) and is regarded as a salient feature of the obesogenic environment (36).

Updating the formula for appetite control: a proposed role for fat-free mass and resting metabolic rate

Over the course of 50 years, scientific thinking about the mechanisms of appetite control has changed dramatically. In the 1950s and 1960s, the hypothalamic 'dual centre' hypothesis was believed to provide a comprehensive account of the intiation and inhibition of food intake e.g. Anand and Brobeck (38). Following technological advances in the identification of neurotransmitter pathways in the brain, the two-centre hypothesis was replaced by a model (proposed by Blundell) which was based on catecholaminergic and serotonergic aminergic systems (39). At the time, this approach was understood to provide a modern and powerful explanation of appetite. Later, with the discovery of families of neuropeptides, the peptide hypothesis of central control of appetite replaced the 'somewhat dated' aminergic ideas. A recent conceptualization has proposed a theory of appetite control based on an interaction between adipose tissue (and prominent adipokines) and peripheral episodic signals from intestinal peptides such as ghrelin, cholecystokinin (CCK), insulin, glucagon-like peptide-1 (GLP-1), peptide tyrosine-tyrosine (PYY), amylin and oxyntomodulin (24). This two-component approach

apparently summarizes current thinking. However, the history of the physiology of appetite control illustrates that any model can be improved by new findings and that some models have to be completely replaced following the advent of new knowledge. Therefore, the current conceptualizations should not be regarded as permanent fixtures; they are transient representations of the current state of knowledge.

Moreover, the current model of appetite control (see above) has been compiled on the basis of evidence from studies directly on the brain (of rats and mice), *in vitro* molecular studies on adipose tissue and experiments on peripheral hormones such as insulin and other gastrointestinal peptides. Not since the work done by Edholm *et al.* (1,2) and Mayer *et al.* (3) in the 1950s has thinking about appetite control taken account of evidence in the field of human energy balance research. Therefore, it is worth considering whether or not any light can be shed on the expression of human appetite from an energy balance approach.

A recent approach to the study of exercise on appetite control has used a multilevel experimental platform in obese humans (40); relationships among body composition, resting metabolism, substrate oxidation, gastrointestinal peptides, sensations of appetite and objective measures of daily EI and meal sizes have been examined. Such a multilevel approach has not previously been undertaken (although it has not been hindered by lack of technology). An important feature of the approach is that all variables have been objectively measured and quantified. This is particularly important in the case of daily EI for which self-report or self-recall do not provide data of sufficient accuracy to be used in assessments of the energy balance budget.

In several cohorts of obese (men and women), the relationship between meal sizes, daily EIs and aspects of body composition (FM and fat-free mass [FFM]) have been measured simultaneously in the same individuals at different time intervals several months apart (41). Contrary to what many would have expected, a positive association was observed between FFM and daily EI, and also with meal size. In other words, the greater the amount of FFM in a person, the greater was the daily energy consumed and the larger the individual meal size (in a self-determined objectively measured eating opportunity). There was no relationship with body mass index (BMI) nor with the amount of adipose tissue (FM) suggesting that, in a free-running situation (with participants not subject to coercive weight loss or dietary restriction), FM does not exert control over the amount of food selected in a meal, nor consumed over a whole day. This outcome is clearly not consistent with an adipocentric view of appetite control. Moreover, the relationships were independent of gender. This means that gender does not explain the association of FFM with EI. On the contrary FFM can explain the gender effect; men (in general) eat more than women because they have greater amounts of FFM.

This association between FFM and eating behaviour has implications for an energy balance approach to appetite control and for the relationship between EE and EI as described by Edholm (1,2). It is well established that FFM is the primary determinant of resting metabolic rate (RMR) and that RMR is the largest component of total daily EE (42). From a homeostatic standpoint, an ongoing and recurring drive to eat arising from the physiological demand for energy (e.g. RMR) appears logical, as this energy demand would remain relatively stable between days and would ensure the maintenance and execution of key biological and behavioural processes. Consequently, it might be predicted that RMR, the major component of daily EE (60–70%) could be associated with the quantitative aspect of eating behaviour and with daily EI. When this was examined (43), it was demonstrated that RMR was a significant determinant of the size of a self-determined meal and of daily energy consumed (when measured objectively and quantified). In addition, RMR was associated with the intensity of hunger objectively rated on handheld electronic data capture instruments (44).

Consequently, these findings – that are broadly consistent with the early predictions of Edholm – have demonstrated an association between the major components of daily EE and daily EI. In other words, they demonstrate that appetite control could be a function of energy balance. Importantly, the major findings have been replicated in completely independent large data sets that included participants from different ethnic groups showing a huge range of EIs (45) and from participants of variable BMIs allowed to freely select their own diet under meticulously controlled semi-free living conditions (Stubbs, Whybrow and Horgan, personal communication). These confirmatory reports suggest that the associations are robust and are not restricted to a particular group of people measured in a specific geographical location.

Considering the strength of the associations, these findings have implications for the role of FFM and RMR in appetite control. They suggest that the conventional adipocentric model should be revised to allow for an infuence of FFM – in addition to FM. The adipocentric feature of the conventional model would be lessened. Our findings do not imply that FM does not play a role in appetite control. Our interpretation is that, under normal weight conditions, FM has an inhibitory influence on food intake but the strength of this tonic inhibition is moderated by insulin and leptin sensitivity (46). As people overconsume (because of cultural obesogenic influences), FM increases and the consequential increase in leptin and insulin resistance weaken the inhibitory influence of FM on appetite. This amounts to a 'dis-inhibition', so that accumulating FM fails to suppress food intake and permits more eating (overconsumption). Indeed, there is good evidence that low insulin sensitivity reduces postprandial
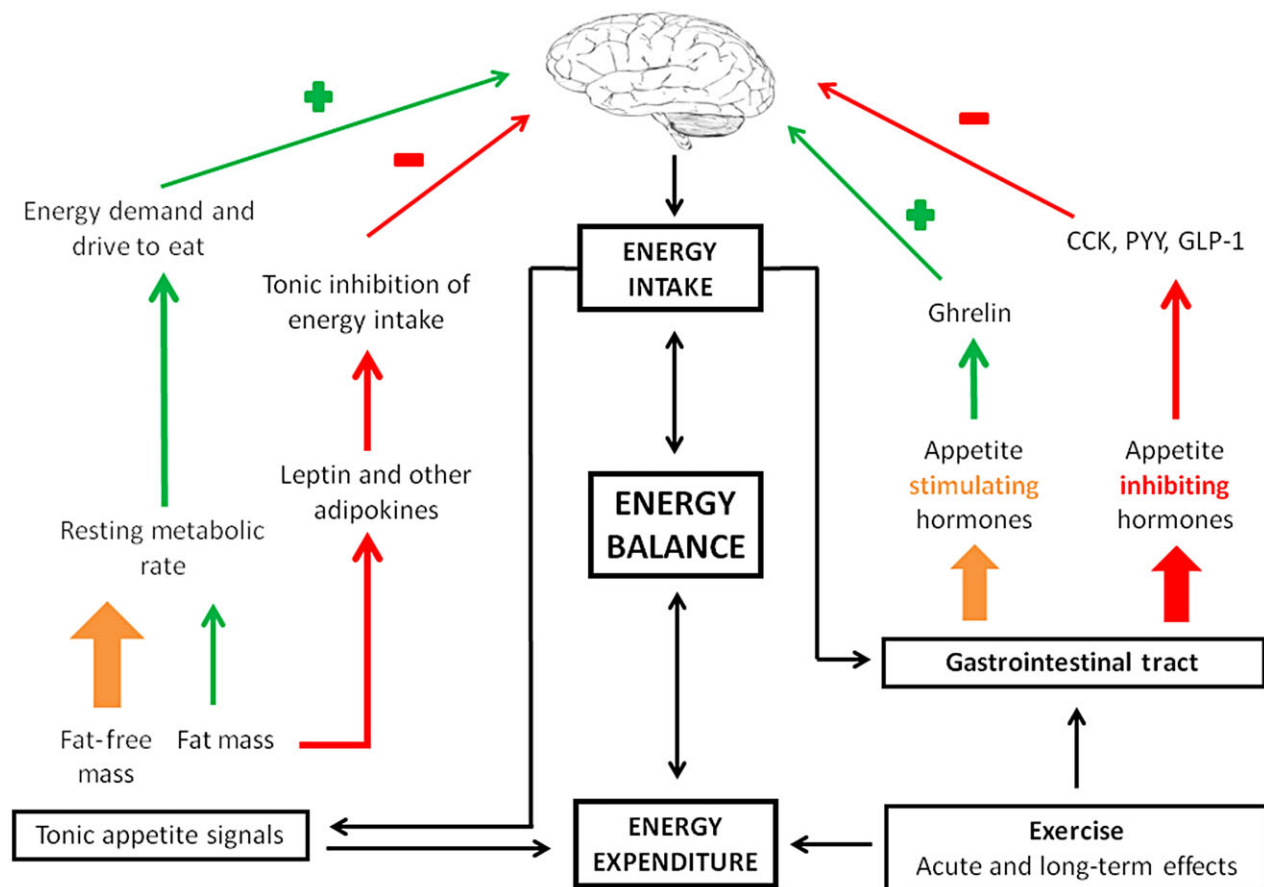
Figure 2 Formulation of the major influences on appetite control using an energy balance framework. There is a distinction between tonic (enduring, relatively stable over days) and episodic (varying in strength during the course of a day) processes. Episodic signals arise as a consequence of food consumption. Tonic signals arise from body tissues and metabolism. The effect of fat mass on energy intake reflects a lipostatic view of appetite control; leptin is a key mediator of the inhibitory influence of fat on brain mechanisms. The metabolic demand for energy arises from energy requirements generated by the major energy using organs of the body (heart, liver, brain, gastrointestinal tract, skeletal muscle) and reflected in resting metabolic rate. The overall strength of the drive for food is the balance between the tonic excitatory and inhibitory processes. It is proposed that, as adipose tissue accumulates in the body, the tonic inhibitory effect of fat on energy intake becomes weaker (due in part to leptin and insulin resistance). Therefore, as people become fatter it becomes more difficult to control appetite. The effect of exercise on appetite control can be understood according to the relative strength of its effects on the tonic and episodic signalling systems (see text).

satiety and weakens meal-to-meal appetite control (47). In addition, clear positive associations of FFM and EI, and negative associations of FM and EI, have been demonstrated – but overlooked – in a comprehensive analysis carried out by Lissner *et al.* (48) more than 25 years ago. Therefore, on the basis of these recent findings, we have proposed a conjoint influence of FFM and FM on appetite control (41). This is set out in Fig. 2. What are the implications of this formulation for the relationship between exercise and appetite control?

Studies on the impact of exercise on energy intake

It should be recognized that studies on the effect of exercise (EE) on EI (appetite) are the converse of studies on the

effect of manipulating EI on EE. Both strategies intervene in an actively regulated physiological system. Considering the impact of a coercive increase in food consumed, a landmark study by Levine *et al.* (49) has demonstrated that a mandatory ingestion of 800 kcal d^{-1} above energy requirements over a 2-month period did indeed lead to an increase in body weight. However, the system tended to oppose this action through an increase in behavioural activity – called non-exercise activity thermogenesis (NEAT). The most striking feature of the study, however, was the wide range of individual responses; some partcipants showed a large increase in NEAT and therefore gained little weight, whereas the opposite was true for others. This outcome calls to mind the results of the Quebec feeding study on monozygotic twins (50). Although members of the twin pairs were equally overfed, the variation in weight gained

Figure 3 Individual changes in body mass and fat mass following a mandatory 12-week exercise programme in which supervised and monitored exercise sessions were given five times per week. The large individual variability shown is typical of the effects seen in other studies using medium-term exercise interventions (13).
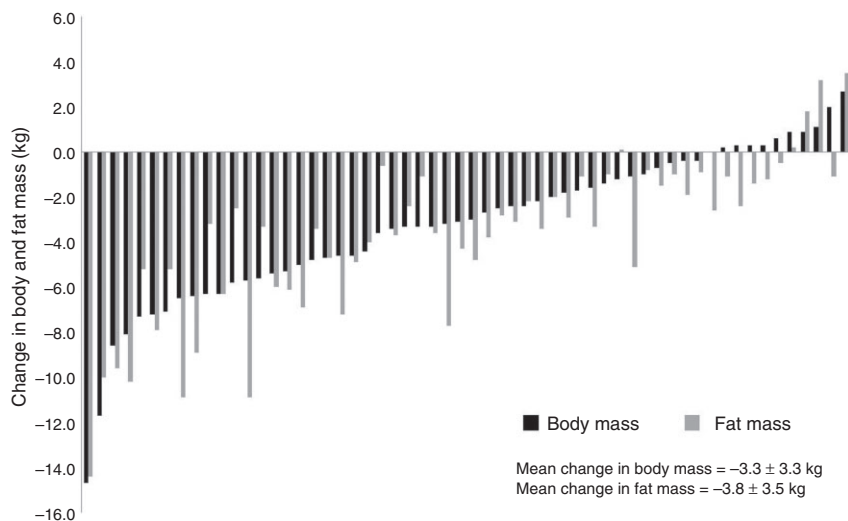
between pairs of twins was large (whereas the variation within any pair of twins was small). Again individual biological variability was pronounced.

What is the case for exercise? Many studies that have assessed EI during the manipulation of exercise have been acute in nature i.e. often single dose, single-day experiments (for a review, see (51) or (52)). The clear outcome is that exercise has little effect on EI within a single day (53). However, as the exercise is continued over several days the system begins to respond and a small compensatory rise in EI has been observed in both men and women (18,54). Comparisons between participants undergoing high, medium and low volume sessions of exercise indicated a graded and proportional (but partial) compensatory increase in EI which accounted for approximately 30% of the EE (18). However, there was a large range of individual variability. This variation became clearer when daily exercise sessions were continued for 16 d with participants showing between 0% and 60% compensation in EI for the exercise EE (54). As anticipated, this variable response was reflected in small changes in body weight.

For medium-term studies, in which mandatory exercise sessions were performed daily for 12 weeks in overweight and obese individuals (13), an average weight loss of approximately 3.3 kg was recorded (the average reduction in body fat was also 3.3 kg) but with weight change varying between −14.7 kg and +1.7 kg. This outcome is quite remarkable because the weight gain of some participants was achieved despite the performance of supervised and measured exercise sessions (5 d per week for 12 weeks). Therefore, even though all participants completed the exercise sessions (with total exercise-induced EE calculated at 28–29,000 kcal), there was a large variation in the change in body composition. The variability in body weight changes following 12 weeks of supervised aerobic exercise has subsequently been replicated in a larger number of

overweight and obese individuals (see Fig. 3) and in several other trials of the effects of PA on weight loss in obese people.

In many studies on the effect of exercise on body weight, the average weight change would be regarded as the most important parameter. However, as several writers including Dilnot (55) have pointed out, science is often weakened by subscribing to the 'tyrany of the average'. The most significant outcome of the study by King *et al.* (13) – and other similar investigations (14) – is the range of individual adjustments in body weight as shown in Fig. 3. This type of outcome is robust and has been demonstrated in different types of participants followed over similar time periods (14). However, more significant than the change in body weight is the effect of exercise on body composition. The weight lost is almost entirely adipose tissue, whereas the weight gain is reflected in lean mass (FFM) which is apparent in both men and women (56).

Exercise and the appetite control system

Can the effects of exercise on body composition be explained by actions on the appetite control system? First of all, it is clear that any compensatory increase in EI, which could offset the exercise-induced EE, is not uniform. Compensation varies markedly from person to person. One reason for this is the observed effects of exercise on different components of appetite control. During medium-term studies, it has been shown that exercise exerts a dual control of the expression of hunger (57,58). First, there is an exercise-induced increase in fasting – or early morning – hunger. However, in contrast, exercise improves satiety by increasing the postprandial sensitivity to ingested nutrients consumed in meals. Interestingly, the increase in postprandial satiety – measured by the satiety quotient or SQ which is an index of the satiating capacity of the energy consumed

(59) – is shown by *all* people who perform the exercise. However, the effect of exercise on fasting hunger is quite variable. Therefore, it can be deduced that the range of the effects of exercise on overall EI is a function of the individual change in basal hunger together with the adjustment in postprandial satiety (57).

A theoretical issue is whether the action of continuous exercise can be understood in the light of recent findings concerning the physiology of appetite control as described earlier. First, the objectively measured responses in appetite behaviour which in turn change EI can be accounted for by the impact of continuous exercise on physiological processes. Because exercise produces adjustments in blood flow, gastrointestinal hormone response, gastric emptying, muscle cellular metabolism, adipose tissue biochemistry as well as brain activity, it will inevitably interfere with several of the mechanisms involved in the episodic control of appetite. Acute responses to exercise-include changes in 'appetite' hormones such as ghrelin, GLP-1 and PYY (60) as well as variable changes in substrate oxidation in muscle and liver may be related to the post-exercise change in hunger and food intake (61).

Second, as exercise is repeated over months, effects on body composition are observed; these normally take on the form of a decrease in FM with maintenace of, or an increase in, lean tissue (FFM) (62). These more gradual changes will bring about adjustments in the tonic control of appetite. Of importance will be a change in resting metabolism (RMR) because of changes in FFM and FM – now shown to be a determinant of meal size and daily EI (43) (as depicted in Fig. 2) and changes in insulin sensitivity (arising indirectly from a reduction in adipose tissue) which influences the accuracy of postprandial satiety (47).

Consequently, it is possible to formulate an account of the way in which exercise can influence body weight. Acute effects of exercise on appetite will be mediated by episodic 'satiety' signals (arising from the act of eating, changes in substrate oxidation (during or imediately after exercise), gastric emptying or other stomach events and skeletal muscle activity (postulated to alter brain dopamine and other transmitters). The effect of enduring exercise will be mediated via changes in body composition in addition to the short-term changes noted earlier. Indeed, the roles of FFM and FM in appetite control seem crucial to an understanding of the action of exercise. Exercise will usually increase FFM and decrease FM. An increase in FFM will increase the demand for energy (to meet increased energy requirements) and this will involve an increase in basal hunger. A decrease in FM will lead to greater postprandial inhibitory control of appetite (satiety) partly by an increase in insulin and leptin sensitivity. Therefore, enduring exercise will lead to an increased sensitivity of appetite control mechanisms. This means that EI will be better matched to EE. However, one consequence of this is that overall EI may be increased.

A summary of the impact of exercise on the control of appetite is set out in Fig. 2. This formulation indicates how the cumulative effect of exercise on body composition (FM and FFM) with implications for hormone sensitivity, together with changes in gastrointestinal peptides responsible for satiety signalling can lead to variable modulation of the compensatory response. The effect of the particular intensity and duration of exercise on an individual person's change in body tissues or hormone release would lead to specific adjustments in the motivation to eat and the satiating response to foods consumed. Consequently, any compensation to prolonged exercise will depend, to a large degree, on the variability of the biological responsiveness between individuals. Therefore, the compensation can be accounted for by the action of exercise on the physiological mechanisms of appetite control. In turn, the biological variation in these mechanisms from person to person can account for the variable effect of exercise on body weight (and body composition).

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Conflict of interest statement

The authors declare no conflict of interest.

References

1. Edholm OG, Fletcher JG, Widdowson EM, McCance RA. The energy expenditure and food intake of individual men. *Br J Nutr* 1955; **9**: 286–300.
2. Edholm O. Energy balance in man. Studies carried out by the Division of Human Physiology, National Institute for Medical Research. *J Hum Nutr* 1977; **31**: 413–431.
3. Mayer J, Roy P, Mitra KP. Relation between caloric intake, body weight, and physical work: studies in an industrial male population in West Bengal. *Am J Clin Nutr* 1956; **4**: 169–175.
4. Jacobs DR. Fast food and sedentary lifestyle: a combination that leads to obesity. *Am J Clin Nutr* 2006; **83**: 189–190.
5. Donnelly JE, Hill JO, Jacobsen DJ *et al.* Effects of a 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women: the Midwest Exercise Trial. *Arch Intern Med* 2003; **163**: 1343–1350.
6. Jakicic JM, Marcus BH, Lang W, Janney C. Effect of exercise on 24-month weight loss maintenance in overweight women. *Arch Intern Med* 2008; **168**: 1550–1559.
7. Ballor D, Keesey RE. A meta-analysis of the factors affecting exercise-induced changes in body mass, fat mass and fat-free mass in males and females. *Int J Obes* 1991; **15**: 717–726.
8. Catenacci V, Wyatt H. The role of physical activity in producing and maintaining weight loss. *Nat Clin Pract Endocrinol Metab* 2007; **3**: 518–529.
9. Borer KT. How effective is exercise in producing fat loss? *Kinesiology* 2008; **40**: 127–138.

10. Shaw K, Gennat H, O'Rourke P, Del Mar C. Exercise for overweight or obesity. *Cochrane Database Syst Rev* 2006; (18): CD003817.

11. Elder S, Roberts S. The effects of exercise on food intake and body fatness: a summary of published studies. *Nutr Rev* 2007; **65**: 1–19.

12. King NA, Hopkins M, Caudwell P, Stubbs RJ, Blundell JE. Beneficial effects of exercise: shifting the focus from body weight to other markers of health. *Br J Sports Med* 2009; **43**: 924–927.

13. King NA, Hopkins M, Caudwell P, Stubbs RJ, Blundell JE. Individual variability following 12 weeks of supervised exercise: identification and characterization of compensation for exercise-induced weight loss. *Int J Obes* 2008; **32**: 177–184.

14. Church TS, Martin CK, Thompson AM, Earnest CP, Mikus CR, Blair SN. Changes in weight, waist circumference and compensatory responses with different doses of exercise among sedentary, overweight postmenopausal women. *PLoS ONE* 2009; **4**: e4515.

15. Hall KD, Sacks G, Chandramohan D *et al.* Quantification of the effect of energy imbalance on bodyweight. *Lancet* 2011; **378**: 826–837.

16. Thomas DM, Bouchard C, Church T *et al.* Why do individuals not lose more weight from an exercise intervention at a defined dose? An energy balance analysis. *Obes Rev* 2012; **13**: 835–847.

17. Stubbs RJ, Sepp A, Hughes DA *et al.* The effect of graded levels of exercise on energy intake and balance in free-living men, consuming their normal diet. *Eur J Clin Nutr* 2002; **56**: 129–140.

18. Stubbs RJ, Sepp A, Hughes DA *et al.* The effect of graded levels of exercise on energy intake and balance in free-living women. *Int J Obes* 2002; **26**: 866–869.

19. Stubbs RJ, Hughes DA, Johnstone AM *et al.* Rate and extent of compensatory changes in energy intake and expenditure in response to altered exercise and diet composition in humans. *Am J Physiol* 2004; **286**: R350–R358.

20. Mayer J. Glucostatic mechanism of regulation of food intake. *N Engl J Med* 1953; **249**: 13–16.

21. Mellinkoff SM, Frankland M, Boyle D, Greipel M. Relationship between serum amino acid concentration and fluctuations in appetite. *J Appl Physiol* 1956; **8**: 535–538.

22. Kennedy G. The role of depot fat in the hypothalamic control of food intake in the rat. *Proc R Soc Lond B Biol Sci* 1953; **140**: 578–596.

23. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. Positional cloning of the mouse obese gene and its human homologue. *Nature* 1994; **372**: 425–432.

24. Badman MK, Flier JS. The gut and energy balance: visceral allies in the obesity wars. *Science* 2005; **307**: 1909–1914.

25. Morton G, Cummings DE, Baskin DG, Barsh GS, Schwartz MW. Central nervous system control of food intake and body weight. *Nature* 2006; **443**: 289–295.

26. Woods SC, Ramsay DS. Food intake, metabolism and homeostasis. *Physiol Behav* 2011; **104**: 4–7.

27. Leibel RL. The role of leptin in the control of body weight. *Nutr Rev* 2002; **60**: S15–S19.

28. Sainsbury A, Zhang L. Role of the arcuate nucleus of the hypothalamus in regulation of body weight during energy deficit. *Mol Cell Endocrinol* 2010; **316**: 109–119.

29. Jequier E, Tappy L. Regulation of body weight in humans. *Physiol Rev* 1999; **79**: 451–480.

30. Chan JL, Heist K, DePaoli AM, Veldhuis JD, Mantzoros CS. The role of falling leptin levels in the neuroendocrine and metabolic adaptation to short-term starvation in healthy men. *J Clin Invest* 2003; **111**: 1409–1421.

31. Schwartz MW. An inconvenient truth about obesity. *Mol Metab* 2012; **1**: 2–4.

32. Norberg M, Lindvall K, Jenkins PL, Emmelin M, Lönnberg G, Nafziger AN. Self-rated health does not predict 10-year weight change among middle-aged adults in a longitudinal population study. *BMC Public Health* 2011; **11**: 748.

33. Egger G, Swinburn B. An 'ecological' approach to the obesity pandemic. *BMJ* 1997; **315**: 477–480.

34. Blundell J, Hill A. Analysis of hunger: inter-relationships with palatability, nutrient composition and eating. In: Hirsch J, Itallie TBV (eds). *Recent Advances in Obesity Research*. Libbey: London, 1985, pp. 118–129.

35. Lenard NR, Berthoud HR. Central and peripheral regulation of food intake and physical activity: pathways and genes. *Obesity* 2012; **16**: S11–S22.

36. Blundell JE, MacDiarmid JI. Passive overconsumption, fat Intake and short-term energy balance. *Ann N Y Acad Sci* 1997; **827**: 392–407.

37. Blundell JE, MacDiarmid JI. Fat as a risk factor for overconsumption: satiation, satiety, and patterns of eating. *J Am Diet Assoc* 1997; **97**: S63–S69.

38. Anand BK, Brobeck JR. Hypothalamic control of food intake in rats and cats. *Yale J Biol Med* 1951; **24**: 123–140.

39. Blundell JE. Is there a role for serotonin (5-hydroxytryptamine) in feeding? *Int J Obes* 1976; **1**: 15–42.

40. Caudwell P, Gibbons C, Hopkins M *et al.* The influence of physical activity on appetite control: an experimental system to understand the relationship between exercise-induced energy expenditure and energy intake. *Proc Nutr Soc* 2011; **70**: 171–180.

41. Blundell JE, Caudwell P, Gibbons C *et al.* Body composition and appetite: fat-free mass (but not fat mass or BMI) is positively associated with self-determined meal size and daily energy intake in humans. *Br J Nutr* 2012; **107**: 445–449.

42. Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C. Determinants of 24-hour energy expenditure in man. Methods and results using a respiratory chamber. *J Clin Invest* 1986; **78**: 1568–1578.

43. Caudwell P, Finlayson G, Gibbons C *et al.* Resting metabolic rate is associated with hunger, self-determined meal size, and daily energy intake and may represent a marker for appetite. *Am J Clin Nutr* 2013; **97**: 7–14.

44. Gibbons C, Caudwell P, Finlayson G, King N, Blundell JE. Validation of a new hand-held electronic data capture method for continuous monitoring of subjective appetite sensations. *Int J Behav Nutr Phys Act* 2011; **8**: 57–64.

45. Weise CM, Hohenadel MG, Krakoff J, Votruba SB. Body composition and energy expenditure predict ad-libitum food and macronutrient intake in humans. *Int J Obes* 2014; **38**: 243–251.

46. Blundell JE, Caudwell P, Gibbons C *et al.* Role of resting metabolic rate and energy expenditure in hunger and appetite control: a new formulation. *Dis Model Mech* 2012; **5**: 608–613.

47. Flint A, Gregersen NT, Gluud LL *et al.* Associations between postprandial insulin and blood glucose responses, appetite sensations and energy intake in normal weight and overweight individuals: a meta-analysis of test meal studies. *Br J Nutr* 2007; **98**: 17–25.

48. Lissner L, Habicht JP, Strupp BJ, Levitsky DA, Haas JD, Roe DA. Body composition and energy intake: do overweight women overeat and underreport? *Am J Clin Nutr* 1989; **49**: 320–325.

49. Levine JA, Eberhardt NL, Jensen MD. Role of nonexercise activity thermogenesis in resistance to fat gain in humans. *Science* 1999; **283**: 212–214.

50. Bouchard C, Tremblay A, Després JP *et al.* The response to long-term overfeeding in identical twins. *N Engl J Med* 1990; **322**: 1477–1482.

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51. Hopkins M, King NA, Blundell JE. Acute and long-term effects of exercise on appetite control: is there any benefit for weight control? *Curr Opin Clin Nutr Metab Care* 2010; **13**: 635–640.

52. Donnelly JE, Herrmann SD, Lambourne K, Szabo AN, Honas JJ, Washburn RA. Does increased exercise or physical activity alter ad-libitum daily energy intake or macronutrient composition in healthy adults? A systematic review. *PLoS ONE* 2014; **9**: e83498.

53. Blundell JE, King NA. Effects of exercise on appetite control: loose coupling between energy expenditure and energy intake. *Int J Obes* 1998; **22**(Suppl. 2): S22–S29.

54. Whybrow S, Hughes DA, Ritz P *et al.* The effect of an incremental increase in exercise on appetite, eating behaviour and energy balance in lean men and women feeding ad libitum. *Br J Nutr* 2008; **100**: 1109–1115.

55. Dilnot A. *The Tiger that Isn't: Seeing through a World of Numbers*. Profile Books: London, 2008.

56. Caudwell P, Gibbons C, Hopkins M, King N, Finlayson G, Blundell J. No sex difference in body fat in response to supervised and measured exercise. *Med Sci Sport Exercise* 2013; **45**: 351–358.

57. King NA, Caudwell PP, Hopkins M, Stubbs JR, Naslund E, Blundell JE. Dual-process action of exercise on appetite control: increase in orexigenic drive but improvement in meal-induced satiety. *Am J Clin Nutr* 2009; **90**: 921–927.

58. Martins C, Kulseng B, King NA, Holst JJ, Blundell JE. The effects of exercise-induced weight loss on appetite-related peptides and motivation to eat. *J Clin Endocrinol Metab* 2010; **95**: 1609–1616.

59. Green S, Delargy HJ, Joanes D, Blundell JE. A satiety quotient: a formulation to assess the satiating effect of food. *Appetite* 1997; **29**: 291–304.

60. Stensel D. Exercise, appetite and appetite-regulating hormones: implications for food intake and weight control. *Ann Nutr Metab* 2010; **57**: 36–42.

61. Hopkins M, Jeukendrup A, King NA, Blundell JE. The relationship between substrate metabolism, exercise and appetite control. *Sports Med* 2011; **41**: 507–521.

62. Lee MG, Sedlock DA, Flynn MG, Kamimori GH. Resting metabolic rate after endurance exercise training. *Med Sci Sports Exerc* 2009; **41**: 1444–1451.

63. Mayer J, Marshall NB, Vitale JJ, Christensen JH, Mashayekhi MB, Stare FJ. Exercise, food intake and body weight in normal rats and genetically obese adult mice. *Am J Physiol* 1954; **177**: 544–548.

64. Blundell JE. Physical activity and appetite control: can we close the energy gap? *Nutr Bull* 2011; **36**: 356–366.