Dual-process action of exercise on appetite control: increase in orexigenic drive but improvement in meal-induced satiety

Neil A King, Phillipa P Caudwell, Mark Hopkins, James R Stubbs, Erik Naslund, and John E Blundell

ABSTRACT
Background: Exercise could contribute to weight loss by altering the sensitivity of the appetite regulatory system.
Objective: The aim of this study was to assess the effects of 12 wk of mandatory exercise on appetite control.
Design: Fifty-eight overweight and obese men and women [mean (±SD) body mass index (in kg/m²) = 31.8 ± 4.5, age = 39.6 ± 9.8 y, and maximal oxygen intake = 29.1 ± 5.7 mL · kg⁻¹ · min⁻¹] completed 12 wk of supervised exercise in the laboratory. The exercise sessions were designed to expend 2500 kcal/wk. Subjective appetite sensations and the satiating efficiency of a fixed breakfast were compared at baseline (week 0) and at week 12. An Electronic Appetite Rating System was used to measure subjective appetite sensations immediately before and after the fixed breakfast in the immediate postprandial period and across the whole day. The satiety quotient of the breakfast was determined by calculating the change in appetite scores relative to the breakfast’s energy content.
Results: Despite large variability, there was a significant reduction in appetite scores relative to the breakfast’s energy content.

INTRODUCTION
The role of exercise in weight management is usually associated with the direct effect of the energy deficit, which in turn creates a negative energy balance and leads to weight loss. However, it is possible that exercise could influence body weight indirectly by exerting some influence on appetite regulation. Although the acute effects of exercise are relatively well understood, the effect of chronic exercise on appetite is less clear. Some studies have shown that habitual exercisers display better appetite regulation than their sedentary, less active counterparts (1). More recently, Martins et al (2) showed that acute appetite regulation improved in sedentary individuals after a 6-wk exercise intervention; however, the exercise was prescribed but not supervised. In the 1950s, Mayer et al (3) examined the issue of physical activity and its benefit for energy balance regulation, and, although no direct effects on appetite were measured, he suggested that physical activity could improve energy balance by regulating appetite. Indeed, it was also proposed that exercise serves to “fine-tune” the appetite regulatory system (4).

One of the criticisms of exercise and its role in weight management is that any exercise-induced energy deficit could automatically be offset by an increased drive to eat (see references 5 and 6 for reviews). Classic physiologic studies have suggested that in the long term energy expenditure and intake fluctuate reciprocally so as to maintain body weight (7). Appetite regulation tends to be sensitive to acute and chronic dietary restriction (8, 9), and there is some evidence that interventions that successfully promote weight loss are accompanied by an increased drive to eat in the fasted state (10–12). However, it should not be assumed that exercise will automatically exert the same effect as dieting. This issue of compensatory responses to exercise has been discussed in detail previously (13). The evidence suggests that acute bouts of exercise do not automatically increase food intake, but there is emerging evidence to suggest that appetite sensitivity is influenced by perturbations in energy balance when exercise is repeated daily with a 9-d (14) or 19-d (15) protocol. There is a need to better understand the behavioral and physiologic consequences associated with modulated appetite sensitivity. This study was designed to determine the effects of a 12-wk exercise intervention on different processes of satiation, satiety, and appetite sensitivity. We hypothesized, on the basis of our previous short-term studies, that despite the imposed exercise being carefully supervised, and thus the assurance that that all

1 From the Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Australia (NAK); the BioPsychology Group, Faculty of Medicine and Health, University of Leeds, Leeds, United Kingdom (PCP and JEB); The Rowett Research Institute, Aberdeen, United Kingdom (JRS); Clinical Sciences, Danderyd Hospital, Karolinska Institute, Karolinska, Sweden (EN); and the Department of Health and Exercise Science, Trinity and All Saints Colleges, Leeds, United Kingdom (MH).
2 Portions of these data were presented at the European Congress on Obesity in Geneva, Switzerland 2008.
3 Supported by the Biotechnology and Biological Sciences Research Council (BBS/B/05079).
4 Address correspondence to NA King, Institute of Health and Biomedical Innovation, Queensland University of Technology, 60 Musk Avenue, Brisbane, Queensland 4059, Australia. E-mail: n.king@qut.edu.au.
Received March 4, 2009. Accepted for publication July 9, 2009.


921
participants achieve a similar exercise-induced energy expenditure, there would be large variability in body weight response. A further hypothesis was that individuals who lost less than the theoretical amount of weight would compensate for the energy deficit by an increased motivation to eat and energy intake.

SUBJECTS AND METHODS

Subjects

Eighty-one participants were recruited for the study; 23 participants did not complete the 12 wk of exercise. Therefore, 58 participants (19 men and 39 women) completed 12 wk of exercise. Their mean (±SD) body mass index (in kg/m²), age, and maximal oxygen uptake (VEO₂max) were 31.8 ± 4.5, 39.6 ± 9.8 y, and 29.1 ± 5.7 mL·kg⁻¹·min⁻¹, respectively. All participants were weight stable (<2.0 kg change in 6 mo) and not taking any medication that would interfere with the measures. Participants and their General Practitioners provided written consent and approval to take part in the study. The study received ethical approval from the Institute of Psychological Sciences Ethical Review Board. Recruitment started in January 2005.

Design

Participants were subjected to a 12-wk obligatory exercise program that was individually designed to expend 500 kcal per session at ≈70% of each individual’s maximum heart rate 5 d/wk under supervised conditions in the research unit. The participants could choose from a range of exercise modes (treadmill running, cycling ergometer, stepping machine, and rowing ergometer) to achieve the target of 500 kcal per session. The duration and intensity of the exercise session were calculated for each individual and recalculated every 4 wk to account for changes in body weight and/or VO₂max. Indirect calorimetry was performed for each participant every 4 wk to measure exercise-induced energy expenditure during the sessions. The dependent variables measured at weeks 0 and 12 are mentioned below.

Fixed breakfast

To assess the acute and chronic effects of exercise on appetite regulation, a probe day food measurement protocol was used, including a fixed breakfast, to enable measurement of the satiety quotient (SQ). The energy content of the fixed breakfast was determined on an individual basis. On the first visit, participants were instructed to eat to a comfortable level of fullness for the breakfast. This determined the fixed amount of energy at breakfast for subsequent testing, including week 12. Therefore, the energy content varied between participants but remained constant within participants. Participants visited the human appetite research unit at 0800 to be provided with the breakfast. The fixed breakfast consisted of cereal with milk, toast with jam and margarine, and tea with milk. The mean (±SD) energy content was 406 ± 4.5 kcal, and the proportions of energy contributed by fat, protein, and carbohydrate were 18.5%, 14.6%, and 66.9% respectively.

Food intake

After the personalized fixed breakfast was consumed, total daily energy intake was directly measured periodically during a probe day protocol in which participants consumed food from ad libitum lunch and dinner test meals and an evening snack box. Therefore, an objective measure of daily energy intake was compiled from the energy consumed in the fixed breakfast and 3 subsequent eating episodes. The list of foods and their energy and macronutrient composition are listed in Appendix A.

Body weight and composition

After an overnight fast, both body weight and body composition were measured at baseline and week 12. Body composition was measured by using air plethysmography (Bodpod, Concord, CA).

Subjective appetite sensations

Immediately before, after, and periodically in between meals, appetite sensations were measured by using visual analog scales on the Electronic Appetite Rating System. Ratings were measured immediately before and after the fixed breakfast and then at hourly intervals until 4 h after the meal. The scales used included hunger, fullness, prospective consumption, and desire to eat, which were first proposed >20 y ago (16).

Satiety quotient

The immediate (satiation) and delayed (satiety) effects of the fixed breakfast were assessed by calculating the SQ. This was achieved by relating the amount of breakfast consumed to the appetite sensations after consumption of the food. The SQ allows actual energy consumed to be related to the subsequent change in appetite ratings. The SQ, therefore, reflects the capacity of the energy consumed to modulate postprandial sensations. The following formula was used:

\[
\text{SQ (mm/kcal) = (rating before the eating episode} - \text{rating after the eating episode}) \times 100
\]

Energy intake

The SQ was developed by Green et al (17), and its use was verified in several studies in male and female participants (18, 19). Because the quantity of the fixed breakfast was determined by each participant, the SQ is an individual measure.

Statistical analysis and treatment of data

For body weight, body composition, fasting appetite sensations, and area under the curve (AUC) appetite sensations, paired t tests were used to compare changes between weeks 0 and 12. For the SQ, a mixed analysis of variance was used with sex and group as the between-subjects factors and time and week as the repeated factors. Independent t tests were used to compare differences between the responders and nonresponders. SPSS software (version 14.0; SPSS Inc, Chicago, IL) was used to perform the data analyses.
RESULTS

Whole sample

Data from 58 participants who completed the 12 wk of exercise are reported. The mean (±SD) proportion of exercise sessions completed was 89.1 ± 10.7%. A different data set from 35 of these participants using an identical exercise intervention was reported previously (20).

Body weight and composition

When data from the whole sample were pooled, mean changes in body weight, fat mass, and waist circumference were 3.2 ± 3.6 kg, 3.2 ± 2.2 kg, and 5.0 ± 3.2 cm, respectively. There was a significant reduction in body weight ($t = 7.456$, df = 57, $P < 0.0001$), fat mass ($t = 8.79$, df = 56, $P < 0.0001$), and waist circumference ($t = 12.1$, df = 56, $P < 0.0001$). Fat-free mass remained unchanged ($t = -0.937$, df = 56, NS).

Hunger and energy intake

The probe day energy intake measures varied among the participants, and the changes in daily intake across the 12-wk period correlated significantly ($r = 0.26$, $P < 0.05$) with the changes in body weight (Figure 1A). When the AUC of the hunger sensations was calculated from the daily profiles of hunger visual analog scale scores, the changes in AUC across the 12-wk period were significantly correlated ($r = 0.46$, $P < 0.001$) with the changes in energy intake (Figure 1B).

Analysis of responders and nonresponders

Examination of the distribution of weight changes at the end of the 12-wk period immediately indicated a wide diversity in individual responses. The measured exercise-induced energy expenditure and body-composition data were used to divide the participants into responders and nonresponders based on their actual weight change compared with that predicted from the measured changes in body composition. Therefore, the terms responders and nonresponders are based on the individuals’ actual body-composition changes relative to their predicted changes and not on their behavioral or metabolic responses. For each participant, predicted energy imbalance was estimated by comparing the cumulative total energy expended (from the monitored exercise sessions) with the changes in fat mass and

![FIGURE 1](https://academic.oup.com/ajcn/article-abstract/90/4/921/4597039)

**FIGURE 1.** Scatter plots of the relation between the change (from 0 to 12 wk) in the area under the curve (AUC) for hunger computed from the daily temporal profile and the change (from 0 to 12 wk) in body weight ($r = 0.26$, $P < 0.05$) (A) and in daily energy intake ($r = 0.46$, $P < 0.001$) (B) measured during the probe days in the research unit. $n = 58$ (32 responders and 26 nonresponders).
fat-free mass. Calculations were based on assumed energy costs of 9540 and 1100 kcal/kg fat mass and fat-free mass, respectively (21). The method used to categorize responders and nonresponders is different from that reported by King et al (20).

With the use of this method, responders were classified as having body-composition changes equal to or greater than the change expected due to the exercise-induced increase in energy expenditure. Nonresponders were classified as those individuals who had body-composition changes less than the change expected due to the exercise-induced increase in energy expenditure. Therefore responders and nonresponders were retrospectively classified by degree of compensation in response to the negative energy balance induced by the exercise. Using this method to classify participants, the ratios of males to females were 9:23 and 10:16 for the responders and nonresponders, respectively (21). The method used to categorize responders and nonresponders was different from that reported by King et al (20).

The range of weight adjustments after 12 wk of the exercise period was 9.2-12.9 kg for the responders (+164 kcal/d), but no change (or even a decline) in the energy expenditure. At the end of 12 wk, the responders differed from the nonresponders in all of these variables, but there was no significant difference in total exercise-induced energy expenditure between the responders and nonresponders (F_{1,56} = 0.01, P = 0.92). The mean proportion of exercise sessions completed for the responders and nonresponders was 91% and 89%, respectively.

The mean fasting and AUC hunger levels at weeks 0 and 12 for the responders are shown in Table 2. The nonresponders showed a significant increase in fasting (t = −3.38, df = 25, P < 0.001) and AUC for daily hunger after 12 wk (t = −3.38, df = 25, P < 0.005). This was the same for desire to eat, fullness, and prospective consumption. Therefore, the nonresponders experienced a significant increase in the motivation to eat after 12 wk of exercise. In contrast, the responders did not show an increase in AUC hunger (t = −1.347, df = 31, Ns), despite a significant increase in fasting hunger (t = 4.019, df = 31, P < 0.0001). The periodic (every 4 wk) change in AUC hunger during weeks 0–12 is shown in Figure 2. When all data were pooled, there was a significant main effect of time (F_{3,147} = 5.974, P = 0.001) and a significant time-by-group interaction (F_{3,147} = 2.76, P = 0.045) but no significant main effect of group (F_{1,49} = 0.645, P = 0.426).

### Fixed breakfast and satiety quotient

In contrast with the changes in fasting hunger, the satiating effect of the fixed breakfast increased over the 12-wk period of exercise. This effect was maintained for 4 h after the meal. The profiles of SQ at weeks 0 and 12 are shown in Figure 3 for the responders and the nonresponders. A similar increase in postprandial satiety was experienced by both the nonresponders and the responders. A mixed analysis of variance, with group and sex as between-subject factors, showed that there were significant main effects of week (F_{3,144} = 3.62, P < 0.0001) and time (F_{4,192} = 122.8, P < 0.0001). There was no significant interaction between week and sex (F_{3,144} = 1.004, P = 0.393) or no significant main effect of sex (F_{1,49} = 3.25, P = 0.08). This was also the same for fullness and the desire to eat.

### DISCUSSION

These data provide novel evidence that the effects of exercise on body weight involve actions on more than one process of appetite regulation. First, exercise causes an increase in fasting and total daily hunger in individuals who do not experience substantial weight loss. Second, a fixed breakfast improves satiation and satiety independent of weight loss. Therefore, a dual process influencing the motivation to eat appears to be in operation. The compensatory increase in the drive to eat in response to weight loss has been reported previously in children (10) and adults (9, 11, 12). However, this is contrary to a finding that fasting and meal-induced fullness increased and decreased.

### TABLE 1

<table>
<thead>
<tr>
<th>Variable and group</th>
<th>Week 0</th>
<th>Week 12</th>
<th>Percentage change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Responders</td>
<td>92.9 ± 12.1*</td>
<td>87.7 ± 12.8</td>
<td>−5.7</td>
</tr>
<tr>
<td>Nonresponders</td>
<td>88.4 ± 20.7</td>
<td>87.5 ± 20.6</td>
<td>−1.0</td>
</tr>
<tr>
<td>Fat mass (kg)†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Responders</td>
<td>34.5 ± 9.8</td>
<td>29.3 ± 10.4</td>
<td>−15.3</td>
</tr>
<tr>
<td>Nonresponders</td>
<td>28.9 ± 8.1</td>
<td>27.7 ± 9.2</td>
<td>−4.7</td>
</tr>
<tr>
<td>Waist circumference (cm)†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Responders</td>
<td>103.0 ± 12.9</td>
<td>97.0 ± 12.7</td>
<td>−5.8</td>
</tr>
<tr>
<td>Nonresponders</td>
<td>99.2 ± 11.4</td>
<td>95.4 ± 10.6</td>
<td>−3.7</td>
</tr>
</tbody>
</table>

† Significantly greater change in responders than in nonresponders, P < 0.05 (ANOVA).
* Mean ± SD (all such values).
* No significant difference between the responders and nonresponders in change in waist circumference (ANOVA).
respectively, after 8 wk of energy-restricted weight loss (22). This indicates a difference between food deprivation–induced weight loss and exercise-induced weight loss. The design of the present study permitted the disclosure of a dissociation between 2 different processes of appetite sensitivity expressed as a function of fasting (before eating) and meal-induced states. This operational difference between the 2 measurement states (fasting and postprandial) is logical. In essence, these are 2 different measures—one reflects the homeostatic energy state after a period of reduced body energy (exercise energy expenditure or food deprivation), and the other reflects the interaction between the physiologic system and the physiologic action of food on satiety signaling (23).

This latter effect was clearly shown because the participants had a higher fasting (before breakfast) hunger level at the end of the 12-wk period, yet a breakfast meal of identical nutritional composition caused a greater immediate reduction in this hunger and maintained the level of suppression until the prelunch measurement period (Figure 3). The exercise regimen apparently raised the sensitivity of the physiologic signaling system, which allowed the same amount of food to realize a greater suppression of hunger. This effect was apparent in both the responders and the nonresponders. This effect may be related to the short-lived anorexic action induced by acute exercise (24–26). The reason why this effect was not apparent at every eating occasion was because subsequent meals were not fixed in energy value (they were ad libitum), which thereby allowed the greater level of hunger (measured by AUC) in the nonresponders (Figure 2) to drive a greater level of food intake (Figure 1).

A similar phenomenon, based on the SQ, was reported in a cross-sectional study designed to assess the power of appetite ratings to predict weight loss. Drapeau et al (27) collated data from several weight-loss intervention studies to show that fasting appetite sensations were strongly associated with body weight

![FIGURE 2. Mean (±SEM) change in daily area under the curve (AUC) for hunger over 12 wk in the responders (who lost a significant amount of body weight) and the nonresponders (who showed substantial compensation for the energy expended in exercise). n = 58 (32 responders and 26 nonresponders). When all data were pooled, there was a significant main effect of time (F3,147 = 5.974, P = 0.001) and a significant time-by-group interaction (F3,147 = 2.76, P = 0.045) but no significant main effect of group (F1,46 = 0.645, P = 0.426). A significant increase in the AUC for hunger was observed between weeks 0 and 12 in the nonresponders (t = −3.38, df = 25, P < 0.005) but not in the responders (t = −1.347, df = 31, NS).]
though all of these studies agreed that 2 separate processes can be detected, the particular effect of exercise on the physiology of energy balance (different from energy or protein restriction) generates specific effects on these 2 processes. One of the theoretical implications of these studies is that the subjective expression of hunger involves at least 2 processes: an underlying orexigenic drive and an immediate food-related response (the postprandial effect).

It may be questioned whether different physiologic mechanisms are involved in these 2 processes. From the data presented here, it is not possible to examine the underlying mechanisms that might explain this dual process of action. However, evidence that describes the neuroendocrine changes in response to exercise and weight loss might be involved (25, 26). The peptides associated with appetite and their associated capacity to act as acute and chronic signals of satiety are likely candidates. In line with the dissociation between fasting and meal-induced motivation to eat is the proposal that appetite peptides exert different effects on fasting and meal-induced responses on hunger (23). Tonic signals arise from tissue stores, whereas episodic signals are closely related to the acute consumption of food (30). Therefore, tonic biomarkers are likely to be closely associated with chronic or behavioral traits for eating, whereas episodic markers are associated with acute fluctuations in motivational state (23). Our findings indicate that, since 2 appetite-modulating processes are induced by repeated exercise sessions, it may not be immediately obvious which measured peptide changes are related to which process—the increased orexigenic drive or the increased postprandial sensitivity.

It is also possible that reductions in physical activity during the nonexercise time might also have contributed to the lower than expected weight loss in the nonresponders. However, we examined this possibility by analyzing accelerometer data collected every 4 wk during free-living probe days (data not shown). These readings indicate that the nonresponders did not alter their nonexercise physical activity, and they were not different from the responders.

These data confirm that exercise has the capacity to alter the sensitivity of the appetite regulatory system via the compensatory response to consumed foods or preloads (1, 2). However, the effect of exercise on appetite regulation involves at least 2 processes: an increase in the overall (orexigenic) drive to eat and a concomitant increase in the satiating efficiency of a fixed meal. These processes do not operate with the same strength in all individuals who undertake exercise. Together, the strength of these 2 processes may determine whether individuals lose weight with exercise or maintain weight through energy compensation.

The authors’ responsibilities were as follows—NAK, EN, JRS, and JEB: contributed equally to the design of the study, data analysis, and manuscript writing; and PCP and MH: involved primarily with the data collection and analysis. These data confirm that exercise has the capacity to alter the sensitivity of the appetite regulatory system via the compensatory response to consumed foods or preloads (1, 2). However, the effect of exercise on appetite regulation involves at least 2 processes: an increase in the overall (orexigenic) drive to eat and a concomitant increase in the satiating efficiency of a fixed meal. These processes do not operate with the same strength in all individuals who undertake exercise. Together, the strength of these 2 processes may determine whether individuals lose weight with exercise or maintain weight through energy compensation.

REFERENCES


APPENDIX A

Energy and macronutrient values (per 100 g) for the ad libitum test meals and snack box

<table>
<thead>
<tr>
<th>Food</th>
<th>Energy kcal/100 g</th>
<th>Fat g/100 g</th>
<th>Protein g/100 g</th>
<th>Carbohydrate g/100 g</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ad libitum lunch</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cream cheese</td>
<td>251.6</td>
<td>24</td>
<td>5.9</td>
<td>3.2</td>
</tr>
<tr>
<td>Crisps</td>
<td>515.8</td>
<td>34</td>
<td>6.5</td>
<td>49</td>
</tr>
<tr>
<td>Bread</td>
<td>229.1</td>
<td>2.5</td>
<td>10.1</td>
<td>44.3</td>
</tr>
<tr>
<td>Lettuce</td>
<td>12.6</td>
<td>0.3</td>
<td>0.7</td>
<td>1.9</td>
</tr>
<tr>
<td>Malt loaf</td>
<td>295.9</td>
<td>2</td>
<td>7.7</td>
<td>65.9</td>
</tr>
<tr>
<td>Margarine</td>
<td>364.9</td>
<td>38.0</td>
<td>0.1</td>
<td>6.0</td>
</tr>
<tr>
<td><strong>Ad libitum dinner</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lasagna</td>
<td>119.6</td>
<td>5.2</td>
<td>4.8</td>
<td>14.3</td>
</tr>
<tr>
<td>Peas</td>
<td>66.2</td>
<td>0.9</td>
<td>6</td>
<td>9.1</td>
</tr>
<tr>
<td>Yogurt</td>
<td>113.2</td>
<td>3.5</td>
<td>4.2</td>
<td>17.3</td>
</tr>
<tr>
<td><strong>Snack box</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chocolate biscuits</td>
<td>471.3</td>
<td>23.3</td>
<td>6.7</td>
<td>62.6</td>
</tr>
<tr>
<td>Cheese biscuits</td>
<td>506.9</td>
<td>28</td>
<td>7</td>
<td>60.5</td>
</tr>
<tr>
<td>Flapjack</td>
<td>432.4</td>
<td>22.8</td>
<td>5.7</td>
<td>54.5</td>
</tr>
<tr>
<td>Apple</td>
<td>46.8</td>
<td>0.1</td>
<td>0.4</td>
<td>11.8</td>
</tr>
<tr>
<td>Banana</td>
<td>94.5</td>
<td>0.3</td>
<td>1.2</td>
<td>23.2</td>
</tr>
</tbody>
</table>