The effects of exercise-induced weight loss on appetite-related peptides and motivation to eat

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Precis: Exercise-induced weight loss increases the fasting drive to eat while improving the sensitivity of the appetite control system.

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Abstract

Context: The magnitude of exercise-induced weight loss depends on the extent of compensatory responses. An increase in energy intake is likely to result from changes in the appetite control system towards an orexigenic environment; however, few studies have measured how exercise impacts on both orexigenic and anorexigenic peptides.

Objective: To investigate the effects of medium-term exercise on fasting/postprandial levels of appetite-related hormones, and subjective appetite sensations in overweight/obese individuals.

Design and setting: Longitudinal study conducted in a university research center.

Participants and intervention: Twenty-two sedentary overweight/obese individuals (age:36.9±8.3years, BMI:31.3±3.3kg/m^2) took part in a 12-week supervised exercise programme (5 times/week, 75% maxHR) and were requested not to change their food intake during the study.

Main outcome measures: Changes in body weight, fasting/postprandial plasma levels of glucose, insulin, total and acylated ghrelin (TG and AG), peptide YY (PYY) and glucagon-like peptide-1 (GLP-1) and feelings of appetite.

Results: Exercise resulted in a significant reduction in body weight and fasting insulin and an increase in AG plasma levels and fasting hunger sensations. A significant reduction in postprandial insulin plasma levels and tendency towards an increase in the delayed release of GLP-1 (90-180 min) were also observed after exercise, as well as a significant increase (127%) in the suppression of AG postprandially.

Conclusions: Exercise-induced weight loss is associated with physiological and biopsychological changes towards an increased drive to eat in the fasting state. However, this seems to be balanced by an improved satiety response to a meal and improved sensitivity of the appetite control system.

Introduction

Increasing physical activity (PA) levels has been proposed as a good strategy to tackle obesity (1;2). However, we have shown that weight loss in response to exercise is neither inevitable nor consistent (3). It is likely that some individuals are susceptible to the weight loss benefits of exercise, while others are resistant.

Almost three decades ago it was proposed that "exercise may stimulate the appetite so that persons who exercise increase their eating and do not lose as much weight as expected" (4). It is generally accepted that the appetite regulatory system will quickly defend impositions that promote a negative energy balance (EB). Metabolic and behavioural compensatory responses, targeting both sides of the EB equation, are likely to influence the magnitude of weight loss in response to exercise. Individual variability in those compensatory responses could partly explain inter-individual variation in exercise-induced weight loss and why some individuals fail to lose weight with exercise (5). It has been proposed that the difficulty in maintaining EB in a weight-reduced state is a consequence of a "compromised appetite control". Weight loss may lead to counter-regulatory adaptations possibly through upregulation of orexigenic (ghrelin) and downregulation of anorexigenic (polypeptide YY (PYY) and glucagon-like peptide-1 (GLP-1)) peptides (6). These peptides are expected to serve as food cues and modulate the expression of feeding behaviour by increasing hunger and EI, in an attempt to automatically restore EB and prevent further weight loss.

We have recently shown that participants who lose less weight than expected in response to a supervised exercise programme experience a compensatory increase in habitual energy intake (EI) accompanied by an increased drive to eat (3). The increase in EI experienced by some in response to an imposed exercise programme could theoretically be driven by an increase in the release of ghrelin, an orexigenic peptide, and/or a blunted release of satiety gut peptides in response to a fixed meal.

Not much research has been devoted to the impact of long-term exercise on the release of appetite-related hormones in the obese population and how that relates to weight loss (7). Although it has already been shown that exercise-induced weight loss induces a compensatory increase in total ghrelin (TG) plasma levels (8-10), no significant changes have been reported on acylated ghrelin (AG) (10;11). This is the molecular form which is able to bind to the growth hormone-secretagogue

receptor, cross the blood-brain barrier and, therefore, exert its orexigenic effects at the hypothalamic level. However, the previous two studies were performed in children and adolescents, and in the latter study no significant changes in body weight were observed (11). Evidence regarding the impact of chronic exercise on the plasma levels of satiety gut peptides is also relatively scarce, particularly in the obese population. However, two studies in adolescents have reported an increase in the release of satiety peptides in response to medium- to long-term exercise (11;12).

The aim of this study was to investigate the effects of a 12-week supervised exercise programme on fasting and postprandial plasma levels of appetite-related hormones, and subjective feelings of appetite in sedentary overweight/obese individuals and to determine if any changes were correlated with the magnitude of exercise-induced weight loss.

Subjects and methods

Participants

Twenty-two overweight and obese healthy sedentary volunteers (eight men and fourteen women) were recruited for this study through advertisements posted at the University and surrounding community. Inclusion criteria were as follows: age between 18-60 years old, BMI between 27-35 kg/m^2, weight stable (<2kg variation in body weight on the last three months), not currently dieting to lose weight, not taking any medication known to affect body weight or appetite, a sedentary lifestyle and a restraint score ≤12 derived from the Three Factor Eating Behaviour Questionnaire (TFEQ) (13). Sedentary lifestyle was defined as not engaged in strenuous work or in regular brisk leisure PA more than once a week or in light exercise for more than 20 minutes/day more than 3 times/week and was assessed through an exercise history relating to the three months prior to the study.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki. All participants gave written consent before enrolling in the study and approval was obtained from the regional Ethics Committee (Midt-Norge, Trondheim, Norway).

Study Protocol

Participants underwent a 12-week supervised exercise programme and were asked to maintain their normal diet throughout the study. Several measurements were performed before and after the intervention including: body weight and composition, maximal oxygen consumption (VO_2max), resting metabolic rate, habitual food intake, fasting and postprandial release of appetite-related hormones and subjective feelings of appetite.

A. Exercise programme

Participants underwent a 12-week exercise programme (5 days a week) consisting of treadmill walking or running. The programme was individually designed in order to induce a 500 kcal energy deficit per session at approximately 75% of their maximal heart rate (maxHR). All exercise sessions were supervised in the research unit. Subjects wore a POLAR (S610, POLAR, Finland) heart rate monitor during each exercise session. To account for changes in fitness and body weight, a submaximal VO_2max test was performed at week 4 and 8 to recalculate the exercise duration needed to induce 500 kcal EE.

B. VO_2max measurement

VO_2max was measured during uphill treadmill walking or running (Woodway PPS 55 Med, Munich, Germany), using the system Oxigen Pro (Viasys Healthcare, Hoechberg, Germany). A warm-up period of 10 min (50-60% of HRmax) preceded the test. A plateauing of oxygen uptake (VO_2), despite increased work load and a respiratory exchange ratio $\geq$1.05 were used as criteria for VO_2max. HR was measured during the test (Polar type 610, Polar Electro, Kempele, Finland) and maxHR was defined by adding 5 beats/min to the highest HR value obtained during the VO_2max test.

C. Body composition

Body composition was measured using Dual-energy X-ray absorptiometry (Dexa, Hologic Discovery-A, Integrity Medical systems Inc, Florida, USA).

146 *D. Resting metabolic rate* (RMR)

147 RMR was measured by indirect calorimetry (Deltatrac II metabolic monitor; Datex-Ohmeda Division,
148 Helsinki, Finland) with the participants fasted and laying supine for 30 min under a ventilated hood.
149 Respiratory Quotient (RQ) was calculated as the ratio of carbon dioxide produced to oxygen
150 consumed.

151

152 *E. Habitual Food intake*

153 Participants were asked to maintain their normal diet throughout the study. This was verified by a
154 three-day estimated food diary (including at least one weekend day) using appropriate photographic
155 booklets and household measures to improve the validity of portion size estimates, before the start of
156 the study and at week 12 of the exercise intervention.

157

158 *F. Blood sampling and subjective measures of appetite*

159 Participants visited the research unit in the fasted state (at least 12 hours fast), before and after the 12
160 week exercise intervention (at least 48 hours after the last exercise session to exclude acute effects of
161 exercise). On each occasion an intravenous cannula was inserted into an antecubital vein. Two fasting
162 baseline blood samples (-10 and 0 minutes) were taken and participants asked to rate their baseline
163 appetite using visual analogue scales (VAS). Participants were then instructed to consume a standard
164 breakfast (time=zero) (consisting of bread, orange juice, milk, cheese and jam: 600 kcal, 17% protein,
165 35% fat, 48% carbohydrate) within 10 minutes. Blood samples were taken at regular intervals for a
166 period of 3 hours (every 15 minutes in the first hour and every half an hour in the second and third
167 hour) and subjective appetite was assessed throughout the morning using VAS. Subjective feelings of
168 hunger ("How hungry do you feel?"), fullness ("How full do you feel?"), desire to eat (How much
169 would you like to eat?) and prospective food consumption (How much do you think you can eat?)
170 were assessed using 10cm self-rated VAS, as previously described (14), before and after breakfast and
171 at every half an hour up to 3h.

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G. Hormone measurement

Venous blood was collected into potassium-oxalate tubes for analysis of glucose and potassium EDTA-coated tubes, containing 500KIU aprotinin (Pentapharm, Basle, Switzerland)/ml whole blood, for the measurement of insulin and gut peptides. Samples were then centrifuged at 2000 g for 10 minutes and plasma analyzed immediately (for glucose) or kept at –20° C for later analyses. For the measurement of AG, 50 µl of a 1 N hydrochloric acid solution and 10 µl of Phenylmethylsulfonyl fluoride (Sigma, Schnelldorf, Germany) (10 mg/ml of isopropanol) was added to each ml of plasma immediately after centrifugation. All samples were batch analysed at the end of the study to reduce inter-assay variability.

Glucose was measured using standard laboratory techniques. Insulin, TG and AG were quantified using human-specific RIA kits (Linco Research, St Charles, USA) and GLP-1 and PYY "in house" RIA methods (15;16). The sensitivity of the assays was 14 pmol/L for insulin, 93 pg/ml for TG, 7.8 pg/ml for AG, 1 pmol/L for GLP-1 and 2 pmol/l for PYY. All samples were assayed in duplicate and baseline and end samples of the same individual were analysed in the same batch. The intra-assay coefficient of variation was of <10% for insulin, TG and AG and <5% for GLP-1 and PYY.

H. Measurement of insulin sensitivity

Fasting insulin sensitivity (S_I), as a percentage of a normal reference population (%S), was calculated using the HOMA2 Calculator version 2.2 (University of Oxford, Oxford, UK) (17).

Statistical analysis

Statistical analysis was carried out using SPSS 15.0 (SPSS Inc., Chicago, IL). All variables were checked regarding their normal distribution using the Shapiro-Wilk test. Statistical significance was assumed at $P<0.05$, unless otherwise stated.

Differences in fasting plasma levels of metabolites/hormones and subjective feelings of appetite between the two blood sampling mornings (before and after the exercise intervention) were assessed by paired sample t-tests. The effect of time and exercise (pre- versus post-intervention) on postprandial levels of metabolites/hormones and subjective feelings of appetite were assessed by a

repeated measures ANOVA. Amplitude of variation for appetite-related hormones was calculated as peak minus nadir. For TG and AG, nadir was defined as the single lowest value following breakfast and peak as the single highest value preceding breakfast (average fasting plasma level). For GLP-1 and PYY, nadir was average fasting plasma levels and peak the single highest value following breakfast.

The areas under the curve (AUC) for plasma levels of appetite-related hormones and subjective feeling of appetite were calculated from before to 180 minutes after breakfast, using the trapezoidal rule. The effect of the exercise intervention on the AUC of each subjective feeling of appetite was assessed used paired sample t-tests. Pearson (or Spearman) correlations were used to test the relationship between changes in the plasma levels of the hormones measured, changes in subjective feelings of appetite and weight loss.

Results

Seven women did not complete the exercise programme for several reasons including pregnancy, injury and time constraints. No significant differences in baseline BMI or fitness levels (VO_2max in ml/kg/min) were observed between completers and non-completers. Results are presented for 15 subjects (7 women and 8 men) with a mean age of 36.9±8.3 years.

Exercise compliance

Participants who completed the intervention exercised at least 80% of the expected sessions (average 89±5.9%).

Anthropometry, body composition, RMR, fitness levels and eating behaviour

Changes in anthropometry, body composition, RMR and fitness levels in the 15 participants who completed the study are shown in table 1. There was a significant reduction in body weight, BMI, body fat (%), total fat mass and RMR and a significant increase in VO_2max after the 12 weeks of exercise ($t=9.46$, d.f.=14, $P<0.0001$; $t=9.11$, d.f.=14, $P<0.0001$; $t=4.65$, d.f.=14, $P<0.0001$; $t=7.981$,

d.f.=14, P<0.0001; t=2.297, d.f.=14, P<0.05 and t=-5.68, d.f.=14; P<0.0001, respectively), but no change in total FFM (t=1.344, d.f.=14, P=0.2).

Habitual energy and macronutrient intake

There were no significant changes in energy (2252±569 vs 2228±667kcal; t=0.17, d.f.=14, NS) or macronutrient intake, assessed by the three-day food diaries, with the exercise intervention.

Plasma metabolites and hormones and insulin sensitivity

- *Fasting plasma levels and insulin sensitivity*

One outlier was removed due to abnormally high levels of AG plasma levels at baseline (214.5 pmol/L for fasting and 44655 pmol/L*min for postprandial total AUC (3.4 and 3.5 SDs away from the mean, respectively)). The fasting plasma levels of the metabolites and hormones measured and insulin sensitivity, before and after the 12-week exercise intervention are displayed in Table 2.

The exercise intervention resulted in a significant reduction in insulin and a significant increase in AG fasting plasma levels (t=3.49, d.f.=14, P=0.004; t=-2,960, d.f.=13, P=0.011, respectively), but no significant changes in glucose, TG, GLP-1 or PYY fasting plasma levels. The exercise intervention resulted also in a significant increase in fasting S_I (t=-5.37, d.f.=13, P<0.0001).

- *Postprandial plasma levels*

Glucose and insulin

A significant main effect of time (F(1.720, 17.197)=9.951, P<0.0001), but no effect of exercise or interaction was observed on glucose plasma levels, which increased from breakfast until t=30 min and decreased afterwards (data not shown). A significant effect of time (F(1.895, 23.819)=25.53, P<0.0001) and exercise (P<0.05), but no interaction, was observed in insulin plasma levels (Fig. 1). Insulin plasma levels increased from breakfast until t=45 min and decreased afterwards and were significantly lower after the exercise intervention.

Appetite-related hormones

A significant main effect of time ($F(7, 91)=21.565$, $P<0.0001$), but no effect of exercise or interaction was observed on TG plasma levels, which decreased from breakfast until t=90 min and increased progressively afterwards (Fig. 2). The amplitude of change in TG plasma levels (peak – nadir) increased, on average, 30% with the exercise intervention (204±123 vs 261±151 pmol/L), but this was not significant (t=-1.519, d.f.=14, P=0.151).

No significant effects of time, exercise or exercise*time interaction were observed on AG plasma levels (Fig. 2). However, a closer analysis of the data revealed no significant effect of time at baseline between fasting at t=90 minutes ($F(2.57, 30.79)=3.14$, $P=0.05$), but a significant effect of time (suppression) at the end of the intervention ($F(1.62, 19.42)=9.79$, $P=0.002$). Moreover, a significant increase (127%) in the amplitude of change in AG plasma levels (peak – nadir) was observed with the exercise intervention (12.4 ± 11.1 vs 28.1 ± 21.4 pmol/L, t=-3.061, d.f.=13, P=0.009).

A significant effect of time ($F(2.599, 33.781)=12.839$, $P<0.0001$), but no main effect of exercise or interaction was observed on GLP-1 plasma levels (see Fig. 3). Total GLP-1 AUC (fasting up to 180 min) did not change with the exercise intervention, but there was a tendency for a higher GLP-1 AUC on the last 90 (90-180 min) and 60 postprandial minutes (120-180 min) after the 12-week exercise intervention compared with baseline (1491±365 vs 1689±430 pmol/L*min, t=-2.242, d.f.=14, P=0.042 and 991±231 vs 1126±248, t=-2.388, d.f.=14, P=0.032, respectively).

A significant effect of time ($F(3.291, 42.789)=10.802$, $P<0.0001$), but no effect of exercise or interaction was observed on PYY plasma levels (see Fig. 3). Total PYY AUC (fasting up to 180 min) did not change with the exercise intervention, but there was a tendency for higher PYY AUC between 120-180 min after the 12-week exercise intervention compared with baseline (798±224 vs 888±211, t=-1.770, d.f.=14, P=0.099).

Subjective feelings of appetite

Fasting state

There was a significant increase in fasted subjective feelings of hunger (4.1±1.6 vs 6.5±2.5cm, t=-3.126, d.f.=14, P<0.01), desire to eat (4.8±1.5 vs 6.4±2.3cm, t=-2.604, d.f.=14, P<0.05) and

prospective food consumption (6.0±1.6 vs 7.1±2.0cm, t=-2.286, d.f.=14, P<0.05), and a significant reduction in fullness feelings (3.5±1.1 vs 1.9±1.5cm, t=3.261, d.f.=14, P<0.01) after the 12-week exercise intervention.

Postprandial state

A significant effect of time (F(3.039, 42.553)=20.910, P<0.0001) and exercise (F(1, 14)=10.901, P<0.01) was observed on subjective feelings of hunger, which increased after the 12-week exercise intervention compared with baseline levels (see Figure 4). A significant effect of time (F(3.425, 47.944)=30.693, P<0.0001) and a time*exercise interaction (F(3.908, 54.707)=4.319, P<0.01), but no main effect of exercise, was observed on subjective feelings of fullness (see Figure 4). A significant effect of time (F(7, 91)=16.724, P<0.0001) and exercise (F(1, 13)=5.517, P<0.05) was also observed on subjective feelings of desire to eat, with a similar pattern to that described for hunger feelings (data not shown). A significant effect of time (F(2.716, 38.027)=17.846, P<0.0001), but no main effect of exercise or interaction was observed on subjective feelings of prospective food consumption (data not shown).

There was a significant increase in the total AUC for hunger (530±310 vs 720±342cm*min, t=-2.920, d.f.=14, P<0.05) and desire to eat scores (601±352 vs 794±375cm*min, t=-2.331, d.f.=14, P<0.05) with the exercise intervention, but no significant change in total AUC for fullness (988±375 vs 1001±324cm*min, t=-0.149, d.f.=14, P>0.05) or prospective food consumption (937±460 vs 998±396cm*min, t=-0.805, d.f.=14, P>0.05).

Relationships amongst weight loss changes, subjective appetite sensations and plasma levels of appetite-related hormones

There was a large variability in exercise-induced weight loss and body composition changes (fat mass (FM and FFM)) ranging from –5.9 to -1.2 kg for body weight, -5.2 to -0.6 for FM and -4.0 to +2.7 kg for FFM. Weight loss was not correlated with baseline (pre-intervention) appetite sensations or appetite-related hormone plasma levels or with the changes experienced in response to the exercise programme.

Discussion

To the best of our knowledge, this is the first study to assess the impact of a medium-term supervised exercise programme on fasting and postprandial plasma levels of both orexigenic (TG and AG) and anorexigenic peptides (GLP-1 and PYY) involved in appetite control, in sedentary overweight/obese individuals. We have shown that even though 12 weeks of exercise, inducing an average 3.5 kg weight loss, significantly increase fasting AG plasma levels and subjective feelings of hunger, it also lead to a tendency for an increase in late postprandial release of GLP-1 and a significant increase in the amplitude of change of AG in response to a fixed meal. It is important to note that because participants were asked not alter their food intake, some dietary restraint was exerted which in turn could have contributed to the outcome. Therefore, the observed changes could not be attributed exclusively to exercise-induced weight loss. Moreover, although it can be argued that the test meal used might not have been large enough to induce significant changes in appetite-related hormones, the energy content of our test meal was higher than that used in other appetite studies (18;19).

Previous studies on the impact of exercise-induced weight loss on appetite-related hormones have reported an increase (8-10) or no change in fasting TG plasma levels (20) and no change in fasting AG plasma levels (10;11); however none had previously measured simultaneously changes in fasting and postprandial plasma levels of TG and AG in overweight and obese adults. Moreover, the only available studies on the impact of chronic exercise on the release of satiety peptides are limited by their short duration (5 days of exercise) (12) and absence of postprandial blood sampling (11). The fact that in these two studies no significant change in body weight were observed (11;12), makes it difficult to compare with the results of the present investigation.

We hypothesize that the type and magnitude of counter-regulatory adaptations in response to weight loss is likely to differ depending on the type of weight loss intervention. There is some evidence to suggest that diet-induced weight loss is associated with a compensatory increase in TG plasma levels and a blunted postprandial release of PYY and GLP-1 (6;19). Our findings suggest that exercise-induced changes are different. Exercise-induced weight loss may increase the drive to eat, as shown by increased levels of AG and subjective feelings of hunger in fasting, but it may also improve satiety consistent with the tendency towards an increase in the late postprandial release of GLP-1. These

findings are in line with our previous observation that even though medium-term exercise-induced weight loss increases both fasting hunger and hunger across the day, it also improves the satiety efficiency of a breakfast (as shown by a significant increase in the satiety quotient) (21). Moreover, we have shown here that the suppression of TG and AG in response to food intake (calculated as amplitude: peak – nadir) increases with exercise, although only significantly for AG. The increase in the amplitude of change of AG observed with the exercise intervention was due to the increase in fasting AG and not to a more pronounced decrease after the breakfast meal. However, it is important to acknowledge that prior to the exercise intervention, when participants were sedentary; AG plasma levels were irresponsive to food intake. This pattern was changed after 12 weeks of exercise with an associated 3.5 kg average weight loss. Unfortunaly reports on the impact of weight loss or changes in physical activity levels on the postprandial release of AG are limited and from our knowledge only one study has looked at the role of body weight on AG postprandial secretion (18). Zwirska-Korczala et al (18) reported a significant suppression of AG following the ingestion of a mixed meal in normal weight women, but not in moderately or morbidly obese women with the metabolic syndrome. These findings are consistent with our results and suggest that obesity is characterised by the maintenance of high levels of AG which may supply a constant feeding drive in these individuals. We have shown that this "abnormal" pattern can be changed with exercise-induced weight loss.

We have also previously reported that exercise improves the ability to adjust EI according to previous food consumption (energy compensation) in both normal-weight (22) and overweight/obese sedentary individuals (Martins, C. Kulseng, B. King, N.A. and Blundell, J.E., submitted). These findings suggest that sedentary individuals suffer from a malfunctioning or insensitive appetite control system which can be ameliorated by exercise.

Another important outcome of this study was the fact that the increase in fasting AG plasma levels and hunger (as well as other appetite) sensations, in response to the 12-week exercise programme, were unrelated with the magnitude of weight loss. This finding challenges the hypothesis that these changes are part of a homeostatic compensatory mechanism to restore EB. If this was the case these changes would be expected to increase with the magnitude of weight loss. However, we are aware that our study has a small sample size and more power is required to detect such associations.

Moreover, since all our participants lost weight with the exercise intervention, it is difficult to speculate if the observed changes were a result of weight loss or exercise *per se*. Only a study with sufficient power and where exercise is performed in EB (by matching the energy costs of exercise with an equivalent increase in EI) and energy deficit can clearly establish if the increase in fasting hunger feelings and AG plasma levels is a result of weight loss (and therefore part of a compensatory homeostatic mechanism) or exercise.

We can conclude that although exercise-induced weight loss leads to an increase in fasting AG and hunger sensations, similar to what has been reported in response to dietary-induced weight loss, exercise appears to balance this increased orexigenic drive by improving the satiety response to a meal and the sensitivity of the appetite control system.

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Figure 1. Insulin plasma levels (pmol/L) over time after breakfast, before (♦) and after a 12-week exercise intervention (□). Values represent means ± SEM for 15 subjects. Repeated measures ANOVA showed a significant effect of time ($P<0.0001$), and exercise ($P<0.05$), but no interactions.

Figure 2. Total ghrelin (TG) (top) and active ghrelin (AG) (bottom) plasma levels (pg/mL) over time after breakfast, before (♦) and after a 12-week exercise intervention (□). Values represent means ± SEM for 15 subjects. Repeated measures ANOVA showed a significant effect of time ($P<0.0001$), but no effect of exercise or interactions for TG and no significant main effect of time, exercise or interactions for AG.

Figure 3. GLP-1 (top) and PYY (bottom) plasma levels (pmol/L) over time after breakfast, before (♦) and after a 12-week exercise intervention (□). Values represent means ± SEM for 15 subjects. Repeated measures ANOVA showed a significant effect of time ($P<0.0001$; $P=0.001$), but no effect of exercise or interactions for both GLP-1 and PYY, respectively.

Figure 4. Subjective feelings of hunger (top) and fullness (bottom) (cm) over time after breakfast, before (♦) and after a 12-week exercise intervention (□). Values represent means ± SEM for 15 subjects. Repeated measures ANOVA showed a significant effect of time ($P<0.0001$), and exercise ($P<0.01$), but no interactions for hunger and a significant effect of time ($P<0.0001$), and a time*exercise interaction ($P<0.01$) for fullness feelings.

Table 1. *Anthropometry, body composition and fitness levels at baseline and the end of the exercise intervention (n=15)*

	Baseline	End
Weight (Kg)	96.1±12.0***	92.6±11.7***
BMI(Kg/m^2)	31.3±2.3***	30.1±2.3***
Body fat (%)	35.3±5.6***	33.5±5.9***
Total fat mass (Kg)	34.1±4.9***	31.2±5.0***
Total free fat mass (Kg)	60.8±11.3	60.2±11.1
RMR (kcal/day)	1830.7±317.3*	1741.7±324.9*
Fitness level VO_2 max (ml/Kg/min)	32.9±6.6***	37.7±5.9***

BMI – Body mass index; RMR – Resting metabolic rate; VO_2 – Maximum oxygen uptake.
Results expressed as mean ± SD. Means sharing the same symbol denote significant differences between baseline and end : * P<0.05, ***P<0.0001

Table 2. *Fasting plasma levels of metabolites and hormones and insulin sensitivity at baseline and the end of the exercise intervention (n=15)*

	Baseline	End
Glucose (mmol/L)	5.2±0.4	5.3±0.3
Insulin (pmol/L)	109.0±68.2**	62.8±24.8**
Total ghrelin (pmol/L)	616.6±271	704.7±303.7
Acylated ghrelin (pmol/L)	37.2±18.2*	51.7±26.0*
GLP-1 (pmol/L)	12.8±6.1	11.7±2.3
PYY (pmol/L)	10.6±5.5	10.3±4.8
S_I (%)	69.5±50.4***	99.4±51.8***

Results expressed as mean ± SD. Means sharing the same symbol denote significant differences between baseline and end (within the same group): * P<0.05, ** P<0.01, ***P<0.0001
S_I (%) - fasting insulin sensitivity as a percentage of a normal reference population

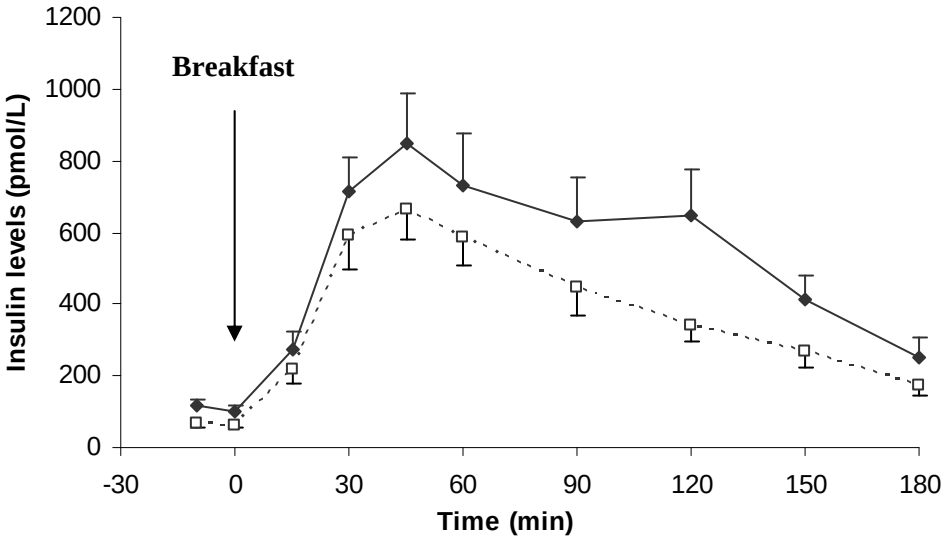
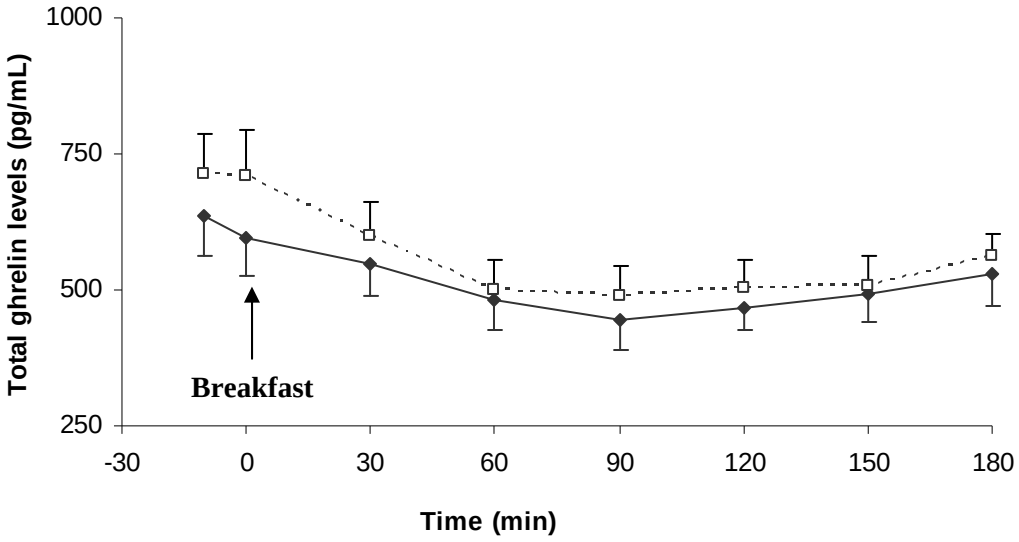
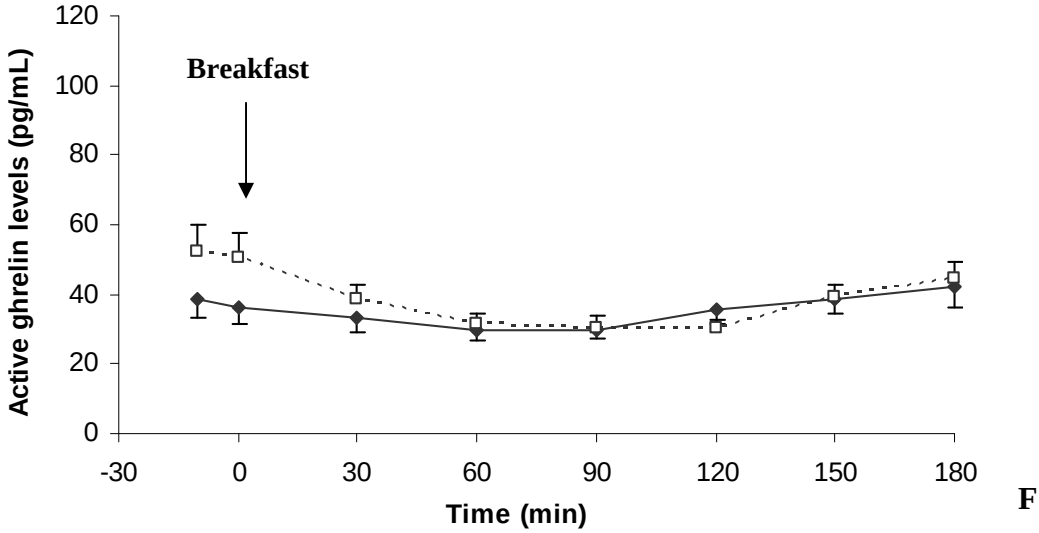

Breakfast
Insulin levels (pmol/L)
1200
1000
800
600
400
200
0
-30
0
30
60
90
120
150
180
Time (min)

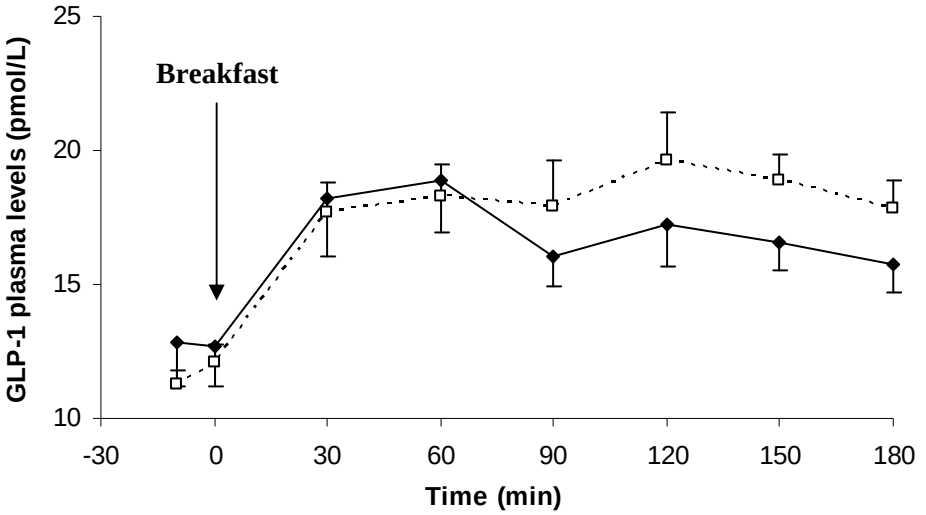
Figure 1.


1000
750
500
250
Total ghrelin levels (pg/mL)
Breakfast
-30
0
30
60
90
120
150
180
Time (min)


120
100
80
60
40
20
0
Active ghrelin levels (pg/mL)
Breakfast
-30
0
30
60
90
120
150
180
Time (min)

F

Figure 2.


Breakfast
GLP-1 plasma levels (pmol/L)
25
20
15
10
-30
0
30
60
90
120
150
180
Time (min)

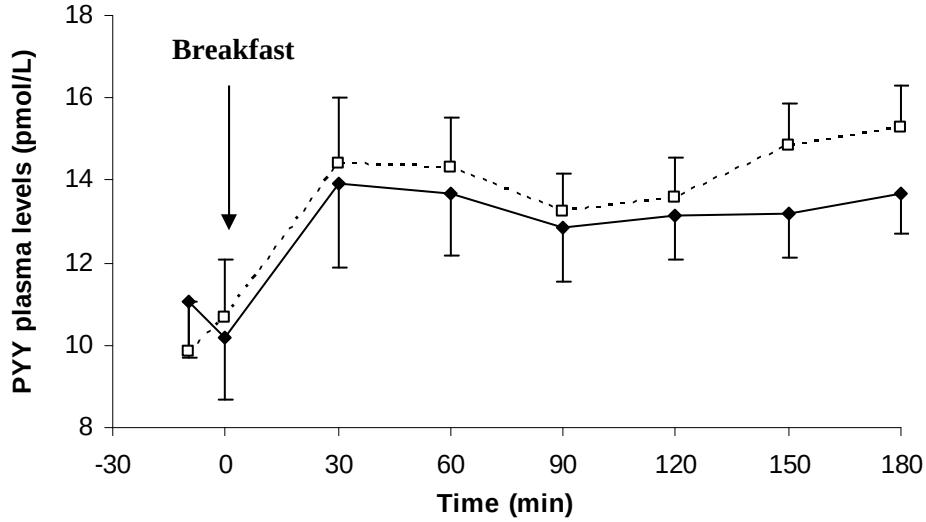

Breakfast
PYY plasma levels (pmol/L)
18
16
14
12
10
8
-30
0
30
60
90
120
150
180
Time (min)

Figure 3.

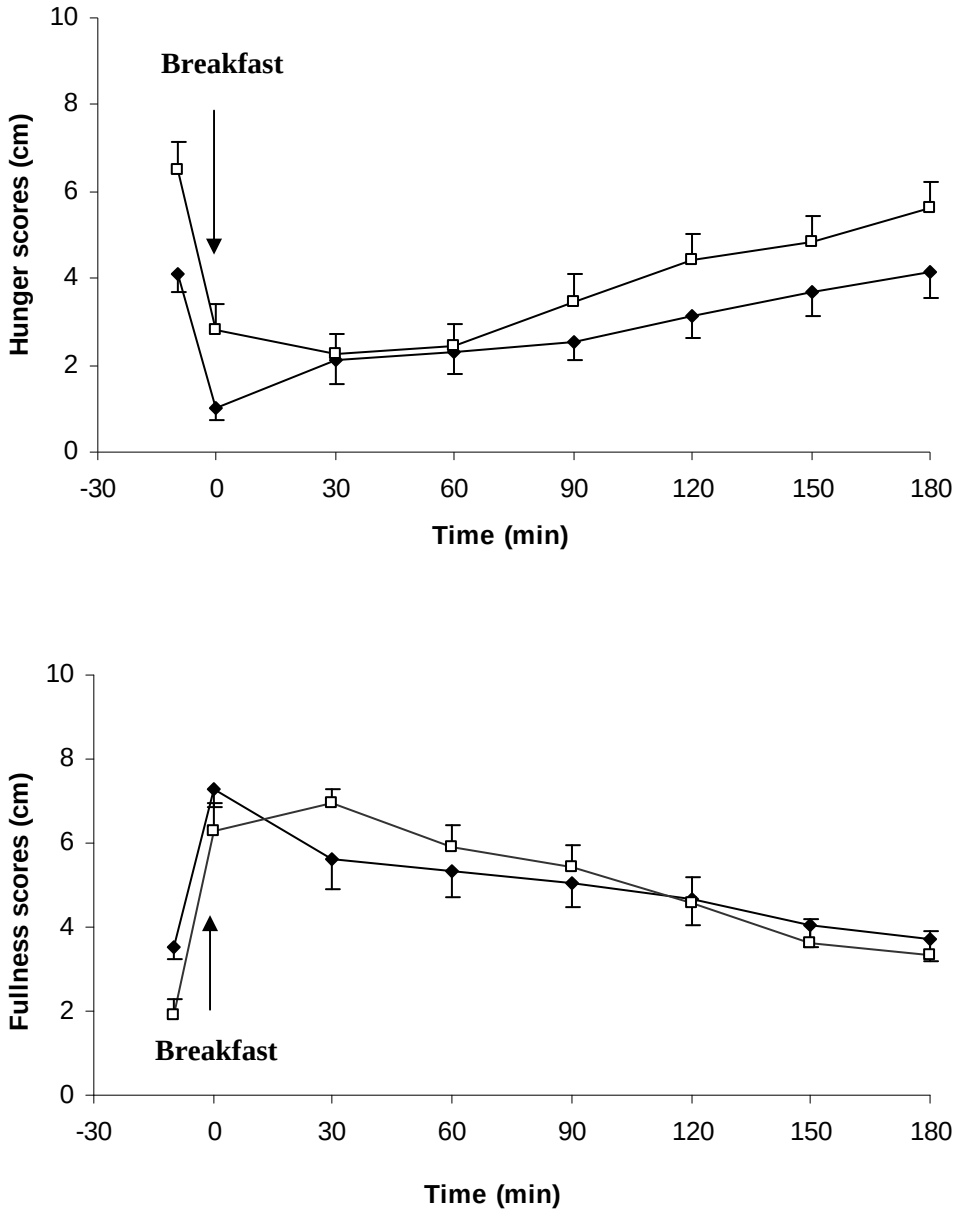

Breakfast
Hunger scores (cm)
Time (min)
Fullness scores (cm)
Breakfast
Time (min)

Figure 4.