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**Title:** The role of episodic postprandial peptides in exercise-induced compensatory eating

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**Abstract**

**Purpose:** Prolonged physical activity gives rise to variable degrees of body weight and fat loss, and is associated with variability in appetite control (hunger and energy intake). Whether these effects are modulated by postprandial 'episodic' peptides is unclear. We examined the role of postprandial peptide response in compensatory eating during 12-weeks aerobic exercise and in response to high (HFLC) and low fat (LFHC) meals.

**Methods:** 32 overweight/obese individuals - 16 completed 12-weeks aerobic exercise and 16 were age- and BMI-matched non-exercising controls. Exercisers were classified as Responders or Non-Responders depending on net energy balance from observed compared to expected body composition changes from measured energy expenditure. Plasma was collected before and periodically after meals to compare profiles of total and acylated ghrelin, insulin, CCK, GLP-1, and total PYY between HFLC/LFHC meals, pre/post exercise, and between Responders/Non-Responders/Controls.

**Results:** No differences in postprandial peptide release was found pre to post intervention. On comparison of exercise Responders, Non-Responders and Controls, greater suppression of acylated ghrelin ($p<0.05$) was found in Responders compared to Non-Responders, along with higher postprandial levels of GLP-1 ($p<0.001$) and total PYY ($p<0.001$) in Responders compared to Non-Responders and Controls.

**Conclusions:** 12-weeks of aerobic exercise training had no impact on postprandial peptide release. Responders to exercise-induced weight loss showed greater suppression of acylated ghrelin and greater release of GLP-1 and total PYY at baseline. Therefore episodic postprandial

peptide profiles appear to form part of the pre-existing physiology of exercise Responders and suggest differences in satiety potential may underlie exercise-induced compensatory eating.

## Introduction

The capacity for exercise to produce an energy deficit puts it at the forefront of many weight loss and weight maintenance programmes [1-3]. However, the reality of exercise producing weight loss is complex, with many exercise intervention studies showing actual weight loss is somewhat less than the predicted weight loss [4]. The individual variability in response to a prescribed, supervised and measured exercise protocol has been documented by different research groups [5, 6]. Furthermore, the fact that some do and some do not lose weight in response to the same stimulus has identified the issue of compensation – which could occur through a number of different mechanisms. Essentially, there are two scenarios – people may compensate for the increased energy expenditure by increasing their energy intake therefore reducing the possibility of weight loss, or they could compensate for the additional physical activity energy expenditure by decreasing their non-exercise activity thermogenesis for the rest of the day, for example by increasing their sedentary behaviour. Much of the research regarding compensation to exercise has focussed on the energy intake side whereby classification of individuals into non-compensators/responders or compensators/non-responders has been investigated [6, 7]. Our group has previously shown that aerobic exercise training affects at least two components of appetite regulation through both increased fasting hunger, but also an increase in satiety [8]. What remains unknown at present is the possible mechanisms implicated in these changes.

One mechanism could be through changes in gut peptides that are related to appetite control. These peptides are generally categorised into ‘tonic’ or ‘episodic’ peptides. Tonic appetite signals are those peptides that are reflective of the body’s energy stores, for example leptin [9], insulin [10] and ghrelin [11]. It is already known that these peptides respond to exercise, and the importance of changes in body composition, particularly in fat mass has been noted [12-

14]; although there is some evidence for an independent effect of exercise, particularly for insulin [15, 16]. In juxtaposition, short-term episodic (meal-related) signals from the periphery fluctuate throughout the day, particularly in response to consumption of food. Ghrelin, primarily involved in meal initiation and glucagon-like peptide 1 (GLP-1), peptide YY and cholecystokinin (CCK) are the primary peptides investigated in response to food consumption. The response of appetite parameters in the period between meals is dependent on the type, quantity and quality of food provided leading to an integrated response via neural and humoral processes [17]. The ability of the gastrointestinal tract to recognise the composition of ingested food is paramount for the maintenance of a stable body weight.

A series of studies have investigated the response of these peptides to an acute bout of exercise [18-23]; yet these studies were predominantly in young, healthy, athletic males and few have investigated the effect of longer periods of training; nor have they recognised the importance of investigating the postprandial peptide response to food before and after aerobic exercise training. Only one study to date has examined the postprandial response before and after a longer term supervised exercise programme [24]. The response to a mixed macronutrient breakfast consisting of 600kcal (17% protein, 35% fat and 48% CHO) was measured before and after the exercise intervention. Insulin sensitivity was found to be significantly higher post-exercise intervention. There was no effect of exercise on total or acylated ghrelin postprandial response to feeding. There was no effect of the exercise on GLP-1 or total PYY postprandial levels, however, the authors reported a trend for higher GLP-1 AUC approximately 2 hours after food consumption and higher total PYY between 120min and 180min after food. There is clearly a lack of studies and consistent evidence in this area therefore the aim of the present study was to investigate the role of postprandial episodic peptides in response to two macronutrient challenges between those who do and do not respond to exercise-induced weight loss. It was hypothesised that responders, non-responders and non-exercising controls may

differ in the postprandial peptide response to high fat or high carbohydrate meals since there is evidence that individual peptides respond differently to the macronutrient composition of the food consumed [25].

Given the large variability in individual obesity treatment programs, identifying variables or components that may help to identify why some people are successful in losing weight compared to those who are not is a clear priority [26].

## Methodology

### Subjects

Thirty-two participants completed the study; 16 (5 males) completed the supervised exercise intervention and 16 (8 males) were recruited as age and BMI-matched controls. All participants were initially screened to ensure they met the inclusion criteria of adults (aged 18-55 years), BMI (27-34.9kg/$m^2$), non-smoking, physically inactive ($\leq$ 2hrs·$wk^{-1}$ of physical activity and not taking part in structured exercise over the previous six months) and not taking medication known to effect metabolism or appetite. Answers on screening questionnaires were verified by researchers during the screening process. All study foods were shown to participants to ensure they liked and would eat all of them and that they had no allergies to any of the foods. None of the participants would be considered restrained eaters using the Three Factor Eating Questionnaire [27]. Participants were recruited from the University of Leeds, UK and surrounding areas using poster advertisements and recruitment emails. The study was conducted in accordance with the Declaration of Helsinki (1964), and all participants provided written informed consent before taking part. Ethical permission was granted by the Leeds NHS Research Ethics Committee number 09/H1307/7 and the School of Psychology Ethics

Committee, University of Leeds. The study was retrospectively registered under international standard trials approval (ISRCTN47291569).

**Exercisers**

Participants were informed of the general nature of the study - an investigation into exercise and appetite-related peptides - but not the precise aims. The time and physical commitments required from them was made clear. Informed written consent was obtained after the nature and possible consequences of the study were explained.

**Non-exercising controls**

Sixteen participants (who were age and BMI-matched to the exerciser group) were recruited. Participants were not made aware of the exercise arm of the study but were informed the research was an investigation into the effect of time on appetite-related peptides. Subjects were requested not to change their dietary or exercise patterns for the duration of the study. All procedures and time commitment was made clear prior to informed written consent being given. Exclusion and inclusion criteria were the same as the exercise group.

**Design**

Participants took part in a 12 week supervised exercise intervention whereby they completed 5 exercise sessions per week, with each session expending 500 kcal which was individually calibrated for each participant. The duration and intensity of the exercise sessions were calculated for each participant and recalculated at week 6 to account for changes in body weight and/or cardiovascular fitness. All exercise was recorded using heart rate monitors, and any sessions missed were added on; this ensured all participants had completed the same amount of energy expenditure before the post intervention measures were completed. Indirect

calorimetry (Vmax Encore, Carefusion) was performed every 6 weeks to measure exercise-induced energy expenditure during the exercise sessions. The intensity was designed to be 'moderate' and was set at 70% of the individual's heart rate maximum (220-age). Participants could choose from a variety of aerobic exercise modes – treadmill walking/running, cycle ergometer, rowing or cross-trainer as long as they kept to their prescribed heart rate. All sessions were supervised within the research unit and recorded using Polar heart rate monitors (RS400).

**Assessment of Maximal Oxygen Uptake**

A maximal fitness test was undertaken every 6 weeks on a treadmill to measure maximum oxygen uptake and calculate the energy expended during exercise. There is a clear linear relationship between oxygen uptake and work rate (heart rate). The treadmill test was incremental until exhaustion using both speed and incline according to a validated $Fat_{max}$ test protocol [28]. The treadmill gradient began at 1˚, with a speed of 3.5km/h. Every three minutes, the speed increased by 1.0km/h until a speed of 6.5km/h was reached. Expired air samples were taken constantly, with heart rate recordings taken during the last minute of the 3 minute intervals. Using the expired air information, if the RQ was lower than one, the incline of the treadmill increased by 2˚ every three minutes. Once an RQ of 1 was reached, the speed of the treadmill increased by 1km/h every minute until exhaustion. Participants were advised to let the researchers know when they thought they were able to continue for only one more minute. Strong verbal encouragement was given to the participant to ensure they reached exhaustion.

**Assessment of Postprandial Peptides**

To assess the acute and chronic effects of exercise on appetite-related postprandial peptides, two probe day measurements were used, one with a high fat/low carbohydrate content (>50%

energy from fat; HFLC) and one with a high carbohydrate/low fat content (less than 3% energy from fat; LFHC). The two probe days were separated by at least 3 days. Participants were provided with a standardised pasta meal on the evening before each test day at week 0 and 12 and were then instructed to fast from 10pm the night before the probe day (with the exception of water). The order of the two conditions was randomised to eliminate a condition effect. Participants arrived at the human appetite research unit at approximately 8am when an intravenous cannula was inserted into the antecubital vein for serial measurements of appetite-related peptides. One fasting blood sample was taken before the participant was provided with breakfast. The breakfasts were matched for energy (590kcal) and weight (685g) but differed in fat/carbohydrate content (High Fat/Low Carbohydrate 50.3% fat, 38.0% carbohydrate and 11.7% protein; High Carbohydrate/Low Fat 3.2% fat, 83.6% carbohydrate and 13.2% protein). Both breakfasts consisted of greek yoghurt mixed with cream, banana, honey, raisins and currants provided to the participant in one bowl to consume together. During pilot testing the breakfast meals were compared on pleasantness and found to be equi-palatable. Participants were given 10 minutes to consume the breakfast therefore matching the rate of consumption between individuals, before serial blood samples were taken at 10, 20 30, 60, 90, 120 and 180 min post-breakfast. During the three hours, participants stayed in the laboratory in separate cubicles to ensure no social influences took place. The cubicles are specifically designed to be devoid of food and time cues so as not to influence the participant.

Samples were analysed for levels of insulin, total and acylated ghrelin, GLP-1, total PYY and CCK. Methods of analysis of these peptides can be found in Gibbons et al, 2013 and Gibbons et al, 2015 [25, 29]. Control group data is not available for total and acylated ghrelin, or CCK; this is because of funding and time constraints limited the number of peptides that could be measured Inter and intra assay coefficients of variation for total ghrelin were 5.9% and 3.4%;

for insulin, GLP-1 and total PYY were 12.5% and 8.3% and for CCK were 15.6% and 9.4%. Insulin data is presented first as an indicator of the sensitivity of the assays used, since it is expected that differences between two conditions will be most prevalent in this biomarker.

**Assessment of Subjective Appetite**

Immediately before each blood sample, appetite sensations were measured using visual analogue scales on a handheld computer [30]. The scales used included hunger, fullness and desire to eat.

**Food Intake**

Three hours after consumption of the fixed breakfast, an ad libitum lunch meal was provided. The lunch consisted of two items, a savoury and a sweet component in order to reflect a normal lunch meal for the study population. This lunch meal was the same on both the HFLC and LFHC conditions, details of the two components can be seen in table 1. Participants were free to consume as much or as little as they wanted until they were comfortably full.

Insert table 1

**Body Composition**

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

**Responder/Non-Responder Classification**

The responders and non-responders were retrospectively classified by degree of compensation in response to the negative energy balance induced by the exercise. The degree of compensation was calculated from measured body composition changes relative to predicted energy imbalance if there was no compensation. Predicted energy imbalance was estimated by summing the energy cost of the exercise over 12 weeks for each individual participant. It was assumed that the energy cost of a 1kg change of fat mass is 39.9MJ (9540kcal) and the energy cost of a 1kg change in lean mass is 4.72MJ (1100kcal)[31]. Using this method participants were divided classified as 'Responders' or 'Non-Responders' by median split. This implies that these individuals had demonstrated differing degrees of compensation for the exercise-induced negative energy balance.

**Statistical Analysis**

Data are reported as mean ± SEM throughout. Statistical analyses were performed using IBM SPSS for Windows (Chicago, Illinois, Version 22). Paired samples t-tests were used to compare fasting levels of peptides to ensure the participants started both days in a similar state. Peptide concentrations were then analysed by repeated measures ANOVA. There was no significant effect of gender on fasting metabolic or appetite hormone levels therefore men and women were analysed together to improve study power. Due to the individual variability in blood parameters and peptide levels the change from fasting at each time point was calculated for each individual as conducted in this lab previously [25, 29]. Mean scores on each peptide outcome were calculated for exercising and non-exercising groups (Group: Responders; Non-Responders; Controls), at baseline and post-12 week intervention (Week: week 0; week 12), before and at 7 further time points after test food intake (Time: 0 min, 10 min, 20 min, 30 min, 60 min, 90 min, 120 min and 180 min), for low fat and high fat probe days (Diet: High fat day; Low fat day). Where significant interactions were revealed, these were explored in follow-up

analyses using the relevant variable combinations. Statistical significance was accepted at a level of $p<0.05$. Where appropriate, Greenhouse-Geisser probability levels were used to adjust for sphericity, and Bonferroni adjustments were applied to control for multiple post-hoc comparisons.

## Results

### Body Composition

The participant characteristics for exercise Responders, Non-Responders and non-exercise Controls can be seen in table 2. There were no differences at baseline between groups. There were no differences in total exercise duration or energy expenditure between exercise groups. Responders lost more weight than Non-Responders and Controls as indicated by differences in weight, BMI, fat mass and waist circumference. The Non-Responders and Controls did not differ over the 12-weeks except for waist circumference which was reduced in Non-Responders after the intervention.

Insert table 2

### Postprandial Peptide Levels

Fasting peptide levels did not change significantly differently between groups in response to exercise. The peptide response to macronutrient composition has been documented previously [25, 29], revealing that insulin showed a greater response to LFHC condition, whereas GLP-1, total PYY and CCK showed a greater response to HFLC. The analysis in the present manuscript

is focussed on the pre to post intervention response, and the group differences in postprandial peptide response.

Insulin

For insulin, there was no main effect of week ($F_{(1,28)}$ 0.623, p=0.436) and no main effect of group ($F_{(2,28)}$ 0.142, p=0.868) or group interactions (figure 1).

Insert figure 1

Total and Acylated Ghrelin

For total ghrelin, there was no main effect of week ($F_{(1,14)}$ 0.068, p=0.798) and no main effect of group ($F_{(1,14)}$ 2.402, p=0.143) or group interactions.

For acylated ghrelin, there was no main effect of week ($F_{(1,13)}$ 0.072, p=0.792) and no main effect of group ($F_{(1,13)}$ 1.004, p=0.335). There was a significant time*group interaction ($F_{(6,78)}$ 4.035, $p<0.05$) and the week*condition*time*group was significant ($F_{(6,78)}$ 2.368, $p<0.05$). Figure 2 indicates that the Non-Responders showed a blunted suppression of acylated ghrelin to HFLC and LFHC breakfasts except after the LFHC breakfast before the exercise intervention where the suppression was similar to the Responders (figure 2).

Insert figure 2

GLP-1

For GLP-1, there was no main effect of week ($F_{(1,29)}$ 0.000, p=0.994) and there was a main effect of group ($F_{(1,29)}$ 11.628, $p<0.001$) but there were no group interactions. The mean peptide concentrations showed a linear trend for Responders to have greater levels of GLP-1 compared

to Non-Responders ($p<0.01$) and Controls ($p<0.001$), while Non-Responders and Controls did not differ significantly ($p=0.162$). Figure 3 indicates no difference between groups over time, but shows that overall Responders showed a greater GLP-1 response.

Insert figure 3

Total PYY

For total PYY, there was a main effect of week ($F_{(1,25)}$ 6.214, $p<0.05$) and a main effect of group ($F_{(1,25)}$ 16.404, $p<0.001$) but no group interactions. The mean peptide concentrations showed a linear trend for Responders to have greater levels of total PYY compared to Non-Responders ($p<0.05$) and Controls ($p<0.001$), and for Non-Responders to have higher levels compared to Controls ($p<0.05$). Figure 4 indicates no difference between groups over time, but shows that overall Responders showed a greater total PYY response.

Insert figure 4

CCK

For CCK, there was no main effect of week ($F_{(1,14)}$ 0.308, $p=0.587$) and no main effect of group ($F_{(1,14)}$ 0.005, $p=0.944$) or group interactions.

**Discussion**

In this study we were able to demonstrate that appetite-related postprandial peptides may be involved in exercise-induced compensation; but that these differences between responders and non-responders precede aerobic exercise training. Responders were characterised by a greater

suppression of acylated ghrelin and greater release of both GLP-1 and total PYY. These differences were observed irrespective of baseline body composition, test meal composition (HFLC and LFHC) or aerobic exercise training suggesting that Responders and Non-Responders have pre-existing differences in physiology that may affect compensatory eating via satiety signalling; and postprandial peptide response (particularly of acylated ghrelin, GLP-1 and total PYY) could be proposed as predictors of weight loss success through aerobic exercise training. Appetite related peptides were clearly responsive to the type of food consumed. In addition they were associated with the degree of weight loss response to prolonged exercise.

In the current study, the energy expenditure was fixed and individually calibrated for each participant, and all exercise sessions were supervised and recorded therefore all participants underwent the same challenge to their energy balance system. Interestingly, the response to this challenge resulted in a large variability in body composition changes, something that has been shown by a number of research groups [5, 6]. There is a growing body of research to support the notion that tonic peptides (that is, peptides related to body weight/body composition) change in response to weight loss. Leptin, insulin and total ghrelin are the forerunners in this evidence and have been shown to respond in particular, to fat loss [32, 33]. There is also evidence of increased insulin sensitivity after exercise training regardless of weight loss throughout the intervention [15]. There is however, little consistent evidence of the response of postprandial peptides, that is, the profile of peptides in response to food both before and after exercise interventions. One study using a similar 12 week exercise intervention found that there was a significant reduction in postprandial insulin, no change in postprandial acylated ghrelin, but a possible trend for increased postprandial GLP-1 and total PYY levels in the late satiety period [24] thereby supporting the evidence for an increase in satiety after aerobic

exercise training. The present study goes a step beyond these findings by demonstrating these differences were present in response to high fat and high carbohydrate meals; and by comparing groups of responders and non-responders in addition to a non-exercising control group.

At present, it is difficult to fully ascertain the role of gut peptides in the control of appetite, particularly when studies using supra-physiological levels are discounted. Current thinking is that some, but not all peptides may be linked to the short term control of appetite [25] and that it is more likely that several peptides are having an accumulative effect on appetite and satiety [29]. This is a logical progression since many peptides are released into the circulation in the fed state therefore co-release of several peptides may more closely represent the physiological fed state. Evidence to support this has been shown in studies co-infusing GLP-1 and total PYY peptides simultaneously has a greater effect on ad libitum food intake than either peptide infused alone [34]. The role of gut peptides in weight loss is substantial, particularly in the literature around obesity surgeries. Support for the findings in the present study can be seen in studies showing that those who experience poor weight loss after Roux-en-Y gastric bypass showed attenuated GLP-1 and total PYY postprandial responses [35]. However, what appears to be a novel finding in the present study is that favourable postprandial peptide profiles of acylated ghrelin, GLP-1 and total PYY at baseline were shown to predict success at exercise-induced weight loss. When the change in variables across exercise interventions are reported in the literature there is often a difficulty in understanding which change occurs first, for example does fat mass decrease before leptin levels decrease. Most people would agree with this direction of events, however it may be that they are occurring concurrently and both are impacting on the other throughout the intervention. The present study supports the idea that those who respond better to exercise have postprandial peptide responses indicative of improved appetite control before they start the exercise which may contribute their ability to

lose weight over the course of the intervention. Of the measured variables in the present study, we found no other predictors of success in these individuals. Future research should investigate the role of free-living physical activity outside of the exercise intervention to assess whether changes have an impact on compensation and weight change in response to an exercise intervention.

Clearly, the exercise intervention was not enough on its own to promote changes in body composition in all individuals; this points towards the possible need for additional dietary or behavioural interventions in some people. It is an interesting proposition that there may be the possibility for identifying individuals beforehand that may or may not be successful in losing weight through exercise by testing the sensitivity of their postprandial peptide response, particularly acylated ghrelin, GLP1 and total PYY. Nevertheless, it must be pointed out that even though the non-responders did not show positive changes in body composition, they did benefit from the exercise intervention through increased fitness and improved health markers (blood pressure/fasting insulin levels) and this message should be communicated rather than changes in weight and body composition. In conclusion, those who lose weight in response to exercise showed a greater suppression of acylated ghrelin and greater release of GLP-1 and total PYY in response to food. These differences were apparent pre and post intervention therefore episodic postprandial peptide profiles may form part of the pre-existing physiology of responders compared to non-responders, and may explain differences in satiety potential underlying exercise-induced compensatory eating.

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494 Table 1. Nutrient and energy composition of the ad libitum lunch

| | **Risotto** | **Yoghurt** |
|---|---|---|
| **Energy (kcal)** | 811 | 810 |
| **Weight (g)** | 480 | 480 |
| **Fat (g)** | 27.6 | 31.0 |
| **Carbohydrate (g)** | 62.3 | 58.7 |
| **Protein (g)** | 10.1 | 10.3 |

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Table 2. Defining body composition characteristics before and after 12 week intervention: Responders, Non-Responders and Controls.

| | **Exercisers** | | | | | | **Non-Exercisers** | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Responders (n=8; 2 males)** | | | **Non-Responders (n=8; 3 males)** | | | **Controls (n=16; 8 male)** | | | |
| | Week 0 | Week 12 | Change | Week 0 | Week 12 | Change | Week 0 | Week 12 | Change | p |
| **Age (years)** | 45.8 (2.7) | | | 45.4 (1.8) | | | 39.6 (2.5) | | | |
| **Weight (kg)** | 83.5 (3.1) | 79.9 (3.1) | -3.6 (0.9) | 90.4 (2.7) | 90.4 (2.6) | 0.0 (0.8) | 93.1 (3.6) | 94.0 (3.8) | 0.9 (0.5) | ** |
| **BMI (kg/m2)** | 29.5 (0.9) | 28.3 (1.1) | -1.2 (0.3) | 30.1 (1.2) | 30.1 (1.3) | 0.0 (0.3) | 30.7 (0.9) | 31.0 (1.0) | 0.3 (0.1) | ** |
| **Fat mass (kg)** | 33.1 (2.5) | 29.0 (3.1) | -4.1 (0.9) | 35.5 (3.3) | 35.0 (3.5) | -0.5 (0.5) | 35.1 (2.2) | 35.8 (2.4) | 0.7 (0.6) | ** |
| **Fat free mass (kg)** | 50.3 (3.1) | 50.8 (3.2) | 0.5 (0.5) | 54.9 (3.4) | 55.4 (3.1) | 0.5 (0.5) | 58.0 (2.7) | 58.2 (2.8) | 0.2 (0.3) | 0.82 |
| **Waist circumf (cm)** | 99.8 (2.0) | 94.8 (2.3) | -5.0 (0.9) | 103.9 (3.3) | 102.0 (3.6) | -1.9 (0.6) | 104.3 (2.0) | 106.2 (2.3) | 1.9 (0.6) | ** |
| **RMR (kcal/d)** | 1740.5 (116.7) | 1714.1 (92.5) | -26.4 (112.7) | 1655.1 (83.1) | 1761.6 (95.3) | 106.5 (78.3) | 1852.1 (83.1) | 1767.9 (96.7) | -149.9 (71.2) | 0.11 |
| **Fitness (ml/kg/min)** | 29.4 (3.6) | 40.9 (3.1) | 11.5 (1.8) | 36.6 (3.1) | 39.9 (2.1) | 3.3 (3.4) | | | | 0.07 |
| **Exercise duration (min/12 wk)** | | 2984.6 (132.6) | | | 2905.9 (167.7) | | | | | |
| **ExEE (kcal/12 wk)** | | 24258.7 (680.9) | | | 24708.3 (1097.0) | | | | | |

*'p' column corresponds to group*time interactions*

*** denotes p<0.01*

*There were no baseline differences between groups*

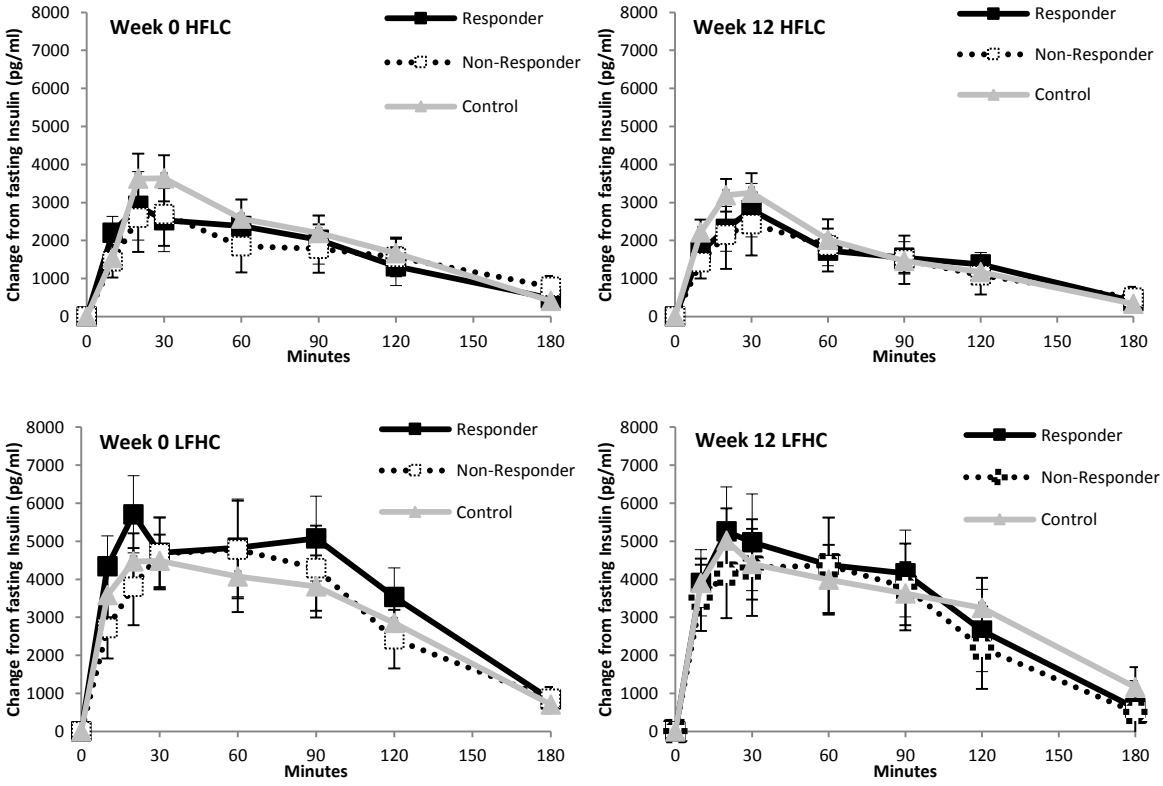


Figure 1. Postprandial profiles of insulin levels in Responders and Non-Responders to exercise and non-exercising Controls during high fat (top row) and low fat (bottom row) conditions before (left column) and after (right column) 12 week intervention.

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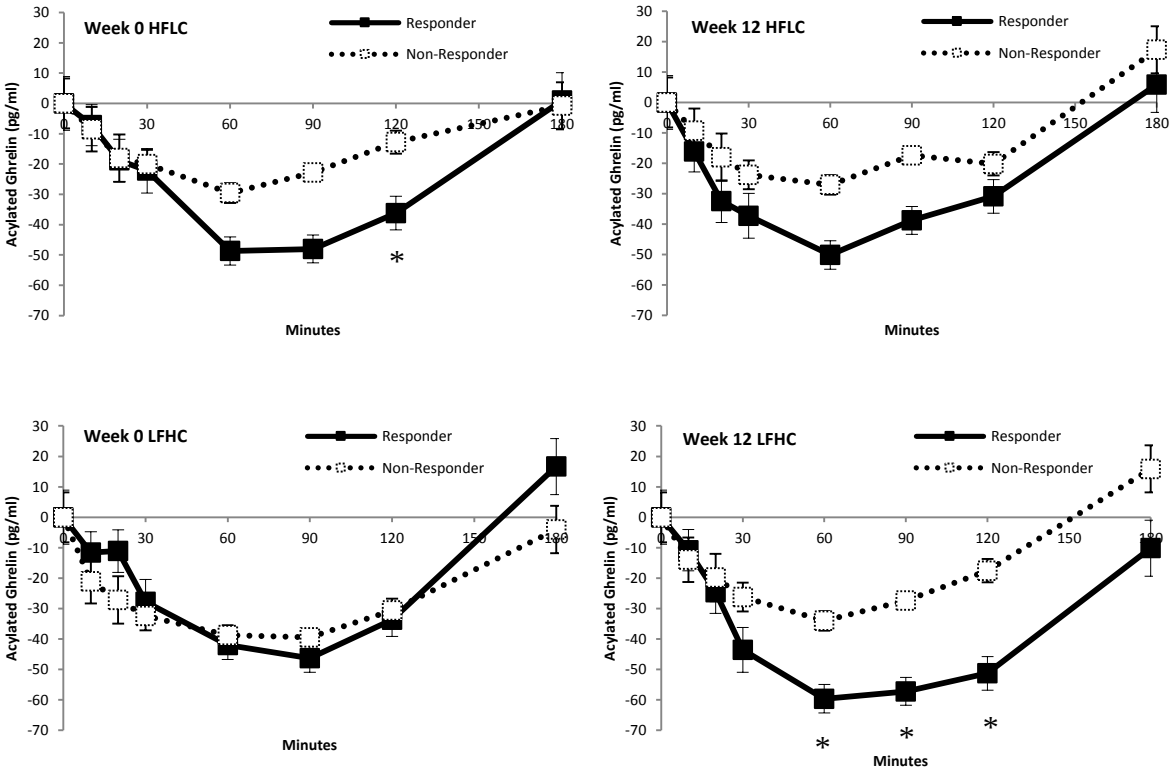


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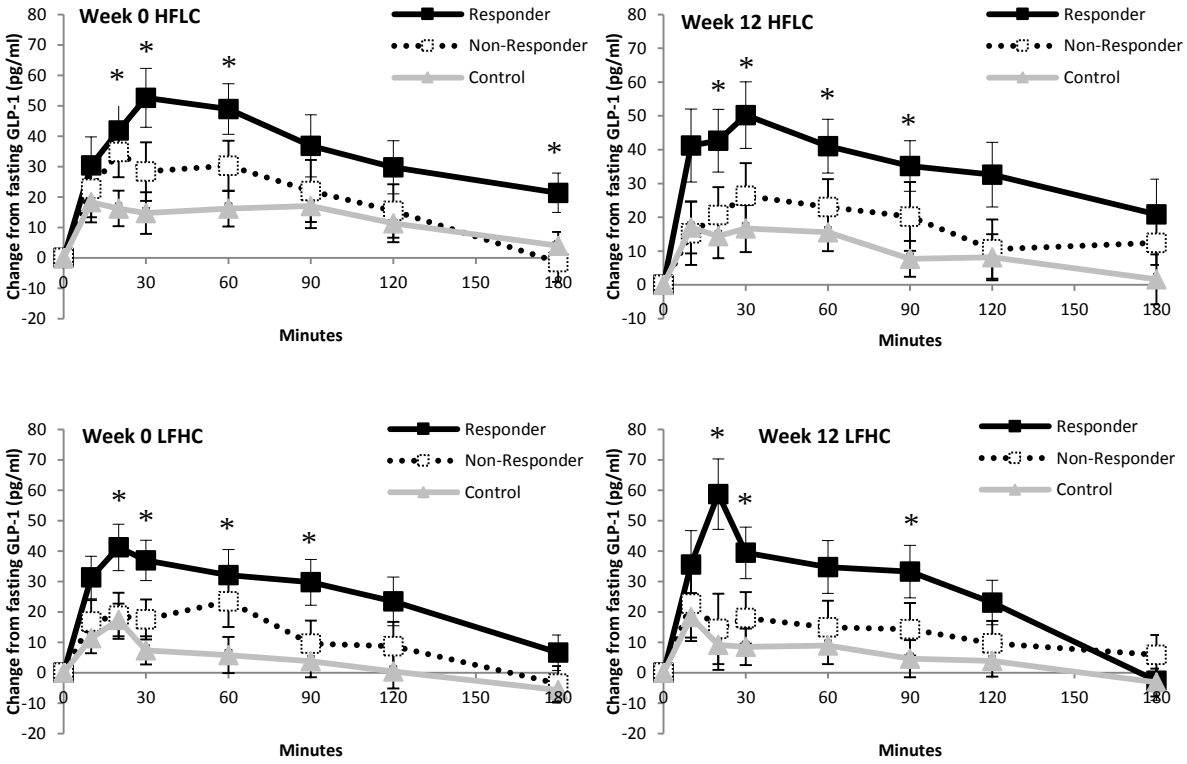
515 Figure 2. Postprandial profiles of acylated ghrelin levels in Responders and Non-Responders
516 to exercise during high fat (top row) and low fat (bottom row) conditions before (left column)
517 and after (right column) 12 week intervention.

518 * Indicates a significant difference between groups at individual time points ($p<0.05$)

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521 Figure 3. Postprandial profiles of GLP-1 levels in Responders and Non-Responders to exercise
522 and non-exercising Controls during high fat (top row) and low fat (bottom row) conditions
523 before (left column) and after (right column) 12 week intervention.

524 * Indicates a significant difference between groups at individual time points ($p<0.05$)

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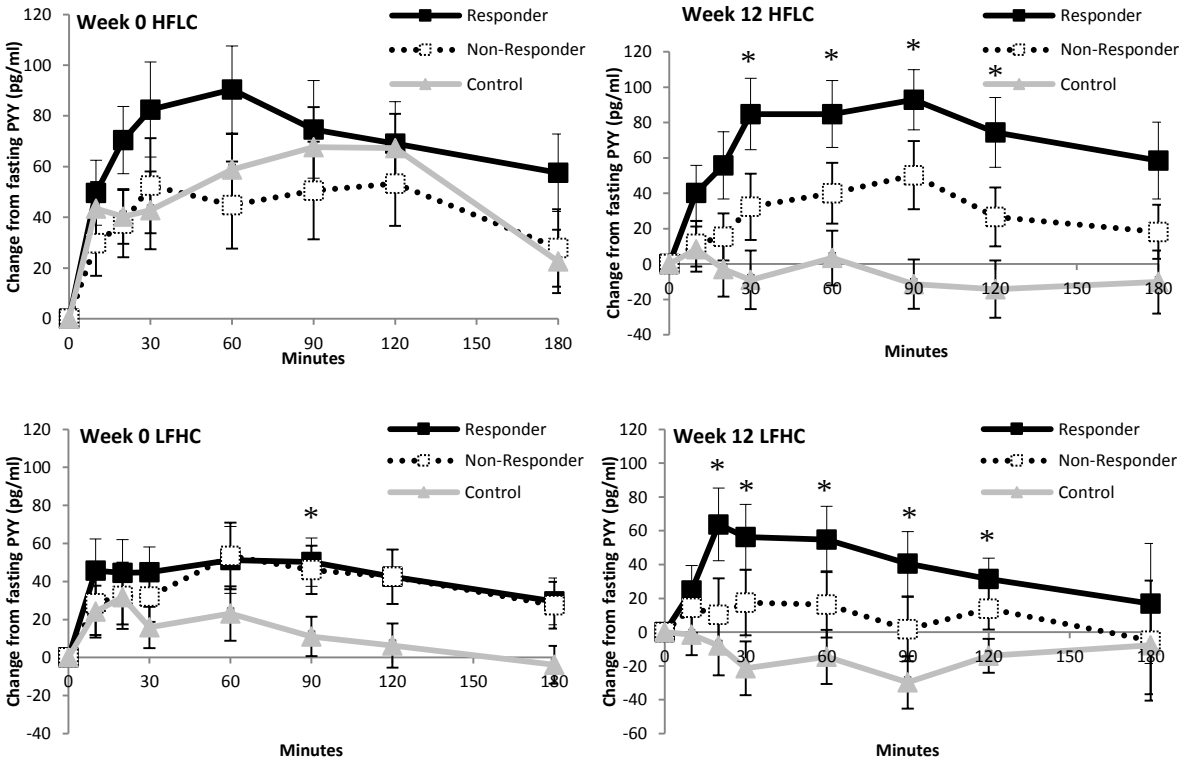


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528 Figure 4. Postprandial profiles of total PYY levels in Responders and Non-Responders to
529 exercise and non-exercising Controls during high fat (top row) and low fat (bottom row)
530 conditions before (left column) and after (right column) 12 week intervention.

531 * Indicates a significant difference between groups at individual time points ($p<0.05$)

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