The Effects of Exercise on Hunger and Satiety Hormone Concentrations Over a 36-Hour Fast: A Randomized Crossover Study

1. Introduction

Food intake and metabolism are often key indicators for the onset of chronic diseases such as diabetes, heart disease and cancer (1). Food intake is largely regulated by hormones that signal satiety and hunger (2). Numerous studies have evaluated how exercise and fasting influence the secretion of these hormones (3,4). Ghrelin is a well known gut hormone that signals a state of hunger to the brain. GLP-1, Leptin, PP, and PYY are known hormones that increase satiation and reduce hunger in humans (5).

It has been found that both an acute bout of exercise, and chronic exercise increases circulating levels of satiety hormones. These changes in satiety hormones influence feelings of satisfaction and decrease food seeking behavior (6). In addition, research in this realm has indicated that intermittent fasting can lead to faster weight loss in obese men and women, but also increases hunger hormones such as ghrelin and reduces satiety hormones such as GLP-1 throughout the fast (7). This hormonal change can influence food consumption, making it difficult to endure the fast.

Currently, there are no studies that we are aware of that couple exercise and fasting to measure the influence on hunger and satiety hormones. Understanding the connection between fasting, exercise and the secretion of these hormones would help determine if and how exercise and fasting should be used together. We aimed to answer this question by measuring hunger (ghrelin, GLP-1, leptin, PP, and PYY) and satiety hormones every 12 hours during a 36-hour fast with and without an initial bout of intense exercise. An additional aim of this study was to measure how subjective ratings of hunger and mood change, and if these ratings are consistent with the expectations gathered from hormonal changes.

2. Materials and Methods

A randomized crossover design with counterbalanced treatment conditions was used to compare the influence of fasting alone to fasting combined with vigorous exercise on the concentration curves of the hormones ghrelin, GLP-1, leptin, PP, and PYY. These two conditions included a 36-hour water-only
fast. The outcome variables were hunger, thirst, stomach discomfort, mood, plasma hormone levels of ghrelin, leptin, glp-1, PP, and PYY.

Participants arrived at the lab having not eaten for four hours. Only water was allowed leading up to the visit. After screenings and assessments, a standardized meal was provided, and a 36-hour fast initiated. Participants were instructed to stay hydrated throughout the fast with water only. Noncaloric, electrolyte, or caffeinated additives were not allowed. Gum chewing was also prohibited.

Based on random assignment, participants either proceeded with a fasting-only regimen or participated in the exercise regimen 30 minutes following the initiation of the fasting period. During the testing period, participants were required to complete hunger and mood assessments every two hours, except during sleeping hours. Additionally, they returned to the lab for venous blood draws every 12 hours beginning at 8:00 pm following the standardized meal.

Body weight and height were measured and participants were asked to rate their mood and energy levels using the Brunel Mood Scale (BRUMS), every two hours. The 24-item BRUMS measures six identifiable mood states (Tension, Depression, Anger, Vigor, Fatigue, and Confusion) through a self-report inventory on a 5-point Likert (8).

Two 4 ml tubes of blood were taken from each participant every 12 hours (time 0, 12, 24, and 36 hours). Hunger and satiety hormone levels were quantified using standard 96-well microplate ELISA kits according to the manufacturer’s instructions.

The energy needs for each participant were estimated using equations validated by Hall et al. (2011). This equation uses height (cm), weight (kg), age (years) and gender to predict basal metabolic rates (BMR). Standardized meals were based on macronutrient content (60% CHO, 25% fat, 15% protein). Participants were given 25% (BMR x 1.55 x 0.25) of their daily caloric requirements in the standardized meal. The same foods were given on both test days and participants were instructed to consume all the food provided for each meal.

Participants exercised on a treadmill at a grade and speed that brought their estimated heart rate reserve (HRR) to 70%. Exercise at this intensity is classified as intense (9) and was used because it has been shown to maximize glucose oxidation during aerobic exercise as compared to lower-intensity training (10). Participants exercised in this manner until an equivalent number of calories was expended.
as given in the standardized meal. The length of exercise was calculated based on the standard ACSM-established metabolic calculation converting oxygen to kcal by multiplying liters of oxygen by 5 (11). All calculations were performed in a preset, protected spreadsheet to ensure accuracy. Energy expenditure was verified using indirect calorimetry.

Area under the curve was calculated using the trapezoidal method. Mixed ANOVAs were used to evaluate differences between conditions and changes in variables over time. Responses from the visual analog scales for hunger, thirst and stomach discomfort were evaluated independently. Significance was set at 0.05. All analyzes were completed using PC-SAS 9.4.

3. Results

Eleven men and nine women were recruited, and all participants completed all aspects of the study. The standardized meal fed to participants prior to each fast was 614.84 ± 85.18 kcal. Measured energy expenditure during the exercise bout on the fast and exercise day was 587.55 ± 120.13 kcal. The average METs during the prescribed exercise was 9.14 ± 1.37. The average respiratory quotient (R) throughout the prescribed exercise was 0.95 (± 0.14), indicating that the major fuel source for the exercise was glucose.(13)

Plasma ghrelin concentrations remained constant for the first 24 hours of the fast and then decreased from 24 to 36 hours. In addition, area under the curve for ghrelin was higher during the fasting only condition compared to the fasting and exercise condition (1456.12 ± 111.10 pg/ml and 1244.31pg/ml ± 111.10 pg/ml (p=0.01), respectively).(see Figure 1A) Plasma GLP-1 concentrations was lower than baseline at hours 12 (p<0.01) and 24 (p=0.04), then rebounded above baseline levels at 36 hours (p<0.01). The area under the curve for GLP-1 was lower in the non-exercise condition compared to the exercise condition (14495 ± 837.58 pg/ml and 16363 ± 837.58 pg/ml (p=0.04), respectfully)(see Figure 1B).

In contrast, plasma leptin concentration was progressively lower at each measurement time point over the 36-hour fast (p<0.01) but area under the curve was not different between conditions (p=0.43). Similarly, both PP (p=0.11) and PYY (p=0.29) were not different between conditions. Plasma PP concentration was lower than baseline at 12, 24 and 36 hours (p’s<0.01). However, at 24 and the 36
hours PP concentrations were higher compared to hour 12 but remained lower than baseline (p’s<0.01). Concentrations of PYY progressively decreased for the first 24 hours and then stayed constant (p<0.01).

Subjective feelings of hunger, thirst, and stomach discomfort were measured using a Visual Analog Scale. While hunger increased over course of the study in both conditions (p<0.01), there was no main effect of condition on hunger, thirst, or stomach discomfort.

**Figure 1 Change in Ghrelin and GLP-1 over a 36-hour fast beginning with or without exercise**

4. Discussion

The results of this study suggest that initiating a period of fasting with a bout of exercise resulted in lower ghrelin and higher GLP-1 concentrations compared to fasting alone. Since, higher levels of circulating ghrelin has a powerful impact on hunger, these results indicate that starting a fast with exercise does not make fasting more challenging but may actually make it easier. This finding is strengthened when combined with the results of GLP-1, which was higher in the exercise condition. GLP-1 has been shown to signal fullness and has a satiating property that can reduce food seeking behavior.

Results from our lab have recently demonstrated that initiating a period of fasting with a bout of exercise significantly accelerates the metabolic changes associated fasting. Specifically, we demonstrated that ketosis was achieved about 3.5 hours faster when a fast was initiated with exercise. Additionally, plasma glucagon concentrations were higher. Taken together, these results with the results of the current study suggest that the metabolic changes associated with fasting can be achieved quicker with exercise and without any negative impact on hunger. In fact, exercise may reduce the biological drive to consume food.

Our results also indicate that objectively measured markers of hunger and satiety do not necessarily match subjective ratings of the same feelings. We observed that perceptions of hunger increase over the course of a fast but there was no difference between conditions. This leads to an
interesting discussion regarding the ability of our sample to accurately assess their subjective feelings of hunger and satiety during an acute fast. The drive to consume food is complex and involves biological drive and a number of cognitive and environmental factors.

5. **Conclusion**

Combining exercise with fasting has a positive impact on ghrelin and GLP-1 during a 36-hour fast. Not only does exercise accelerate metabolic changes during a fast, the results from this study show that biological markers of hunger are decreased. The results may inform individuals participating in a variety of approaches to fasting (alternate day fasting, intermittent fasting or time restricted feeding may), possibly making the behaviors more sustainable over time.
References


