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Impact of Exercise Timing on Appetite Regulation in Individuals with Type 2 Diabetes

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Abstract

Purpose—Exercise improves appetite regulation, but it is not known if pre or postmeal exercise more effectively improves appetite regulation in individuals with type 2 diabetes. For the first time, this study compared how pre and postmeal exercise alters appetite regulation in individuals with type 2 diabetes.

Methods—Twelve obese individuals with type 2 diabetes performed three different trials, all in a random order, in which they consumed a dinner meal with 1) no resistance exercise (RE), 2) premeal RE, or 3) postmeal RE beginning 45-min after dinner. A visual analog scale was used to assess perceived hunger and fullness and frequent blood samples were drawn for determination of acylated ghrelin, pancreatic polypeptide (PP), and peptide tyrosine tyrosine (PYY) concentrations.

Results—Premeal RE increased premeal perceived fullness, reduced perceived hunger, and reduced acylated ghrelin concentrations compared to the no RE and postmeal RE trial ($P<0.05$). In the postprandial period, both pre and postmeal RE reduced perceived hunger compared to no RE, while only postmeal RE reduced postprandial perceived fullness ($P<0.05$) compared to no RE. Pre or postmeal RE did not alter PYY concentrations. In both the premeal and postprandial period, RE reduced PP concentrations compared to no RE ($P<0.05$), but upon cessation of RE, PP concentrations rebounded to concentrations that were similar to no RE.

Conclusion—Both pre and postmeal RE reduced perceived hunger and increased perceived fullness, effects that may help control food intake and aid in weight management efforts in individuals with type 2 diabetes.

Keywords

Physical activity; weight training; hunger; fullness; gut hormones; obesity

Introduction

The regulation of appetite (i.e. drive to eat, hunger) and satiety (i.e. control of meal size, fullness) requires a complex, integrated physiological process that involves numerous gut

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Conflict of Interest

We have no conflict of interest. Results of the present work do not constitute endorsement by ACSM.

and pancreatic hormones. The initiation of hunger is partly mediated by ghrelin, which is the only known anorexic hormone. In circulation ghrelin exists in two endogenous isoforms including acylated or des-acylated ghrelin (5). Acylated ghrelin is the active form of the peptide in circulation, and has the most impact on appetite whereas des-acylated ghrelin has no impact on appetite (5). During fasting, plasma concentrations of acylated ghrelin increase to stimulate hunger, whereas upon meal ingestion acylated ghrelin concentrations decrease to reduce hunger (10). The initiation of fullness is partly mediated by the hormones pancreatic polypeptide (PP) and peptide tyrosine tyrosine (PYY). During fasting PP and PYY concentrations decrease to reduce fullness and promote energy intake, whereas upon meal ingestion plasma PP and PYY concentrations rapidly rise to stimulate sensations of fullness and signal meal termination (3, 4).

In the context of obesity and type 2 diabetes, altered responses of these hormones occur. For instance, in individuals with type 2 diabetes, fasting plasma ghrelin concentrations are typically lower and decrease less in response to a meal (11, 17, 18). Fasting and postprandial PP and PYY concentrations are lower in obese subjects (20, 21), and individuals with type 2 diabetes have been shown to have impaired postprandial fullness (18). These unfavorable changes in appetite and satiety regulation are not permanent, as an acute session of aerobic exercise has been shown to increase postprandial fullness in individuals with type 2 diabetes, without altering acylated ghrelin concentrations (18). Further, we found that short-term aerobic exercise training increased postprandial PP concentrations (16) and intermittent exercise reduced hunger and increased satiety in obese non-diabetic subjects (15).

Although aerobic exercise is commonly prescribed to individuals with type 2 diabetes, another mode of exercise that is often prescribed is resistance exercise (RE) due to its favorable effects on lean body mass and glycemic control (8). Yet, it is not understood how RE influences perceived appetite, satiety, or appetite and satiety regulating hormones in individuals with type 2 diabetes. Further, the optimal time to perform RE relative to meal ingestion (i.e. pre vs. post meal RE) to improve appetite and satiety regulation is not well understood. Therefore, the aim of this study was to examine, for the first time, the impact that RE timing (pre vs. postmeal RE) has on postprandial perceived appetite, satiety, and the appetite and satiety regulating hormones acylated ghrelin, PYY, and PP. Previous studies in non-diabetic individuals shows that RE in the fasted state prior to a meal reduces acylated ghrelin concentrations (2, 6) and perceived hunger (6), increases PP concentrations (2), but does not alter PYY concentrations (2, 6) or subsequent postprandial responses or food intake (2, 6). Furthermore, another study in non-diabetic men showed that aerobic exercise performed after a meal extended the appetite suppressing effect of food intake, and this effect was associated with elevated PYY concentrations (9). Based on these previous findings, it was hypothesized that premeal RE would lower premeal acylated ghrelin concentrations and perceived hunger, increase PP concentrations, not change PYY concentrations, and would not alter subsequent postprandial acylated ghrelin, PP, or PYY concentrations or perceived hunger or fullness. Furthermore, we hypothesized that postmeal RE would extend the appetite suppressing effect of dinner to a greater extent compared to premeal RE, and that this effect would be associated with greater postprandial PYY concentrations.

Methods

Participants

This study was approved by the University of Missouri Health Science Institutional Review Board and participants provided written informed consent. Inclusion criteria for this study included obese (body mass index $> 30 \text{ kg/m}^2$), diagnosed with type-2 diabetes (by physician), not using tobacco products, receiving standard medical care but not using insulin, no history of surgery for weight loss, and weight stable. While participating in this study, the participants took their medication at the usual dose, frequency, and time.

General Experimental Design

This study was part of another study that has been published (14). Prior to beginning experimental testing, the participants completed baseline testing which included assessments of height, weight, body composition (assessed via the BODPOD®), resting energy expenditure, physical activity energy expenditure, and familiarization and strength testing. After completing the baseline testing measurements and in a random order, the participants completed three, 2 d trials (**Figure 1**). On day one of each trial the participants reported to the lab sometime between 3-8 p.m. and a continuous glucose monitor (CGM) was inserted as described previously (14) and the subjects were given their prepackaged breakfast and lunch meals for the next day. On day two of each trial the participants consumed the prepackaged breakfast between 6-8 a.m. and lunch between 11-1 p.m., and consumed these meals at a time they normally eat these meals and at the same time during each trial. Later on that evening, the participants reported to the lab for testing sometime between ~3-5 p.m., and reported at the same time during each trial. Upon arrival, a venous catheter was inserted into a forearm vein and frequent blood samples were taken over the entire testing period. The participants were in the lab for ~6 h total and consumed a dinner meal sometime between ~5-7 p.m. with either 1) no resistance exercise (NoRE, remained sedentary during the testing period), 2) premeal RE (RE-M, ~45 min of RE was performed prior to the meal, with the RE session ending ~20-30 min prior to the meal), or 3) postmeal RE (M-RE, ~45 min of RE beginning 45 min after meal termination).

Resistance Exercise Sessions

The participants performed baseline orientation and strength testing prior to completing the experimental testing trials so that they were accustomed to RE before the study. The participants completed two orientation sessions separated by a 10 repetition maximum (10-RM) strength testing session.

Visit 1—The first orientation session was intended to teach the participants how to correctly execute each exercise. During this session, the weight used for RE was low (~10-40% of bodyweight) and the participants performed 1-2 sets of 10-repetitions of the following exercises (in this order): leg press, seated calf raises, seated chest flyes, seated back flyes, back extensions, shoulder raises, leg curls, and abdominal crunches.

Visit 2—Within 1 week of the first orientation session, the participants returned to the lab for determination of their 10-RM for each exercise described previously (except abdominal crunches).

Visit 3—Approximately 3-7 d after 10-RM testing, the participants reported back to the lab for a second orientation session in which they performed three sets (1-2 min rest between sets) of 10-repetitions for each RE. During this exercise session, the first set executed for each exercise was a warm-up set and the weight used was ~50% of the participants 10-RM. The weight for the next two sets was the participant's previously determined 10-RM weight. The participants completed three sets for each exercise before moving onto the next exercise.

Experimental testing visits—After the first three visits, the participants completed the three experimental study days described previously (**Figure 1**). During the experimental study days, the RE session protocol was identical to the protocol described for the second orientation session.

Diet

To estimate total daily energy expenditure (TDEE), indirect calorimetry (ParvoMedics TrueOne® 2400) was measured to determine resting energy expenditure, and the BodyMedia® armband (BodyMedia, Inc) was used to measure the average physical activity energy expenditure over a 2-3 d period. The participants were provided with their respective TDEE needs during each experimental testing day. For each meal given to the subjects, the macronutrient composition was ~50% carbohydrate, 35% fat, and 15% protein and consisted of commonly eaten foods (14). The breakfast meal (585 kcal) consisted of an English muffin, cheddar cheese, one large egg, ham, hash browns, ketchup, and apple or orange juice. The lunch meal (582 kcal) consisted of white bread, ham, mayonnaise, cheddar cheese, a granola bar, and apple or orange juice. The dinner meal was spaghetti noodles, spaghetti sauce with beef added, garlic bread, a lemon-lime flavored soda, and 1.5 g of acetaminophen (was used to assess gastric emptying in the parent study, ref 14). The total energy provided in the dinner meal was calculated by subtracting 1167 kcal (from breakfast and lunch meals) from the estimated TDEE for each participant. Since the participants consumed the breakfast and lunch meals outside of the lab on their own, compliance and timing of meal ingestion was checked with a continuous glucose monitor (CGM) that was inserted (14). Spikes in glucose indicated the participants consumed a meal, and the timing of the meal was recorded in the CGM software. Further, the subjects kept written records of when they consumed each meal and verbally confirmed they consumed only the meals provided. The subjects were compliant with eating the meals and ate them at roughly the same time of day during each trial.

Metabolic data, Perceived Exertion During Exercise, and Subjective Appetite and Satiety

During the time frame (~45-47 min) when RE was performed, indirect calorimetry (Parvo Medics TrueOne 2400) was used to measure energy expenditure and substrate oxidation. The BORG 6-20 scale was used to assess the participant's ratings of perceived exertion at

the end of every RE set. Subjective hunger and fullness were measured using a 100-mm visual analog scale after every blood draw as described previously by our lab (13).

Blood Collection and Plasma Separation

Frequent blood samples were taken throughout testing. A blood sample was drawn every 5-10 min during the first ~3.7 h of testing and every 30 min during the final 2 h, but not all of these samples were assayed for acylated ghrelin, PP, and PYY concentrations. Prior to the meal, three blood samples were assayed for these hormones including the baseline sample, a sample taken ~30 min prior to the dinner meal (which was close to the end of the RE session during the RE-M trial), and a sample taken immediately prior to the dinner meal. After the dinner meal was consumed, the blood samples taken at 30, 60, 90, 120, 150, 210, and 240 min after the meal were assayed for appetite and satiety hormones. Blood samples were transferred immediately into chilled EDTA tubes with added aprotinin (ThermoFisher Scientific, Inc.), dipeptidyl peptidase-4 inhibitor (Millipore Corp.), and Pefabloc® SC (DSM Nutritional Products AG) to prevent the breakdown of acylated ghrelin, PP, and PYY. Blood was separated into plasma by spinning at 1,409 g for 10 min at 4°C and the plasma was frozen at -80° C until analysis.

Biochemical Analyses

A MILLIPLEX magnetic bead-based immunoassay (Millipore Corp.) was used to assess plasma acylated ghrelin, PYY, and PP hormone concentrations. After every blood draw, hematocrit was measured and all samples were corrected for plasma volume shifts. Calculation of the plasma volume variations (% VP) were computed using hematocrit variations (Ht, Ht1 = baseline Ht, Ht2 = sample after baseline Ht) with the following formula: $\% VP = 100 * [(Ht1 - Ht2) / (Ht2 * (100 - Ht1))]$. Hormone values corrected for plasma volume shifts were computed using the following formula: Corrected hormonal value = (Initial Value*100) / (100 - % VP). For all assays, the inter- and intra-assay coefficient of variation was < 10%.

Calculations and Statistical Analysis

The incremental area under the curve (*iAUC*) was computed, as described by Pruessner et al. in Microsoft Excel (23), and used to quantify postprandial responses. The *iAUC* controls for variations in fasting hormone / substrate concentrations when subjects are measured over repeated study days and more accurately describes the postprandial response (7, 23). GraphPad Prism 6 (GraphPad Software, Inc.) was used to perform the statistical analysis. To determine statistical significance in metabolic, heart rate, and perceived exertion data between RE trials, a paired samples t-test was used. To test for statistical significance between the *iAUC* values between trials, a one way repeated-measures ANOVA with follow-up Holm-Sidak *post hoc* tests were used. To test for statistical significance between individual time points, a two way repeated measures ANOVA was used, and if a significant interaction was found follow-up Holm-Sidak comparisons were made to identify specifically where statistically significant differences were. Alpha was set at $P = 0.05$, the data is for $N = 12$, and expressed as means $\pm$ S.E.M. unless otherwise noted.

Results

Participant Characteristics and Metabolic and Perceived Exertion Data During Exercise

Twelve men and women with type 2 diabetes were recruited for this study (**Table 1**). All participants were obese, physician diagnosed with type 2 diabetes, not using insulin, and undergoing standard medical care. During exercise, the duration of each session, oxygen consumption, energy expenditure, the respiratory exchange ratio, and average RPE were not different between the pre and postmeal RE sessions (**Table 2**). Average heart rate was ~5 beats per minute higher during postmeal RE compared to premeal RE.

Perceived Appetite (Hunger) and Satiety (Fullness) Responses

There were no significant differences between pre ($P = 0.27$) or postprandial ($P = 0.23$) perceived hunger *iAUC* values between trials (**Figure 2A, B, C**). For individual time points, there was a significant interaction ($F = 1.55$, $P = 0.05$). At the time point immediately prior to the meal, perceived hunger was ~14-17% lower during the premeal RE trial (60 ± 8 mm) compared to the NoRE trial (73 ± 5 mm, $P < 0.01$) and M-RE trial (70 ± 6 mm, $P = 0.01$), suggesting that premeal RE attenuates the rise in hunger. The time point corresponding to 100 min after the meal (and at approximately the end of exercise during the M-RE trial) was ~45% lower ($P = 0.03$) during the M-RE trial (12 ± 2) compared to the NoRE trial (22 ± 5), and was ~33% lower compared to the RE-M trial (18 ± 6), but this did not reach statistical significance ($P = 0.21$). At the time points corresponding to 210 and 240 min after the meal, perceived hunger was significantly lower during both RE trials (RE-M trial: time point 210 = 23 ± 5 mm, $P = 0.03$; time point 240 = 26 ± 6 mm, $P = 0.001$; M-RE trial: time point 210 = 19 ± 4 mm, $P = 0.002$; time point 240 = 25 ± 5 mm, $P = 0.001$) compared to the NoRE trial (time point 210 = 33 ± 6 mm, time point 240 = 39 ± 7 mm), suggesting that both pre and postmeal RE extend the appetite suppressing effect of a meal.

The premeal perceived fullness *iAUC* was significantly greater during the RE-M trial (43 ± 336 mm · 100 min, $P = 0.04$) compared to the M-RE (-999 ± 381 mm · 100 min) and NoRE (-1021 ± 337 mm · 100 min) trial, indicating that premeal RE increases perceived fullness (i.e. attenuates the drop in fullness prior to a meal) (**Figure 2D, E, F**). The postprandial perceived fullness *iAUC* was not significantly ($P = 0.08$) different between trials. However, for individual time points, there was a significant interaction ($F = 1.66$, $P = 0.05$). The individual time points corresponding to -45 min ($P = 0.03$), -35 min ($P = 0.01$), -25 min ($P = 0.02$), and -5 min ($P = 0.02$) prior to the meal were significantly greater during the RE-M trial compared to the NoRE trial, but were not different compared to the M-RE trial ($P = 0.08$). The individual time point at 210 min after the meal in the M-RE trial (73 ± 4 mm) was ~22% greater ($P = 0.03$) compared to the NoRE trial (60 ± 6 mm), and was ~12% greater compared to the RE-M trial (65 ± 6 mm), but this was not significantly different ($P = 0.22$). Furthermore, the individual time point at 240 min after the meal in the M-RE trial (69 ± 5 mm) was ~33% ($P = 0.002$) and 21% greater ($P = 0.03$) compared to the same time point in the NoRE (52 ± 7 mm) and RE-M (57 ± 5 mm) trials, respectively, indicating that postmeal RE reduces postprandial perceived satiety (i.e. extends the satiety effect of dinner).

Hormonal Responses

The premeal acylated ghrelin *iAUC* was significantly lower during the RE-M trial ($-2,005 \pm 752$ pg/ml $\cdot$ 100 min) compared to the NoRE trial (-186 ± 130 pg/ml $\cdot$ 100 min, $P = 0.03$) and M-RE (585 ± 547 pg/ml $\cdot$ 100 min, $P = 0.004$) trial (**Figure 3A, B, C**), indicating that premeal RE suppressed acylated ghrelin concentrations prior to the meal. Conversely, the postprandial acylated ghrelin *iAUC* was significantly greater during the premeal RE trial ($-1,012 \pm 537$ pg/ml $\cdot$ 100 min) compared to the NoRE ($-9,180 \pm 2,298$ pg/ml $\cdot$ 100 min, $P = 0.02$) and M-RE ($-12,969 \pm 3,021$ pg/ml $\cdot$ 100 min, $P = 0.01$) trial (**Figure 3**), indicating the drop in acylated ghrelin after meal ingestion was less because at the start of the meal acylated ghrelin concentrations were lower compared to the other trials. For individual time points, there was a significant interaction effect ($F = 10.31$, $P < 0.01$). At the time point corresponding to -35 min prior to the meal (and close to the end of RE during the RE-M trial), acylated ghrelin was significantly different between all trials ($P < 0.01$) (**Figure 3A**). In addition, the individual time point corresponding to -5 min prior to the meal was $\sim 39\%$ and $\sim 41\%$ lower during the RE-M trial (64 ± 12 pg/ml) compared to the NoRE (104 ± 18 pg/ml, $P = 0.0001$) and M-RE (108 ± 18 pg/ml, $P = 0.0001$) trial, respectively. At the time point corresponding to 30 min after the meal, acylated ghrelin was $\sim 89\%$ and $\sim 72\%$ greater during the NoRE trial (98 ± 14 pg/ml) compared to the RE-M (52 ± 7 pg/ml, $P < 0.01$) and M-RE (57 ± 8 pg/ml, $P < 0.01$) trial, respectively. At 90 min after the meal, acylated ghrelin concentrations during the M-RE trial (33 ± 5 pg/ml) were $\sim 38\%$ lower compared to the RE-M trial (53 ± 10 pg/ml, $P = 0.02$), but were not significantly different compared to the NoRE trial (47 ± 8 pg/ml, $P = 0.12$).

The pre or postmeal PP or PYY *iAUC* was not significantly ($P > 0.05$) different between trials (**Figure 3D, E, F**). Furthermore, for individual time points there was a significant interaction effect for PP ($F = 2.55$, $P < 0.01$), but not for PYY ($F = 0.92$, $P = 0.55$) (**Figures 3G, H, I**). At the individual time point corresponding to -35 min prior to the meal, PP concentrations were $\sim 36\%$ lower ($P = 0.01$) during the RE-M trial (169 ± 41 pg/ml) compared to the M-RE trial (264 ± 66 pg/ml), but were not significantly different compared to the NoRE trial (249 ± 69 , $P = 0.66$). At the individual time points corresponding to 30 min and 90 min after the meal, PP concentrations were $\sim 20\text{--}24\%$ lower during the M-RE trial (30 min = 329 ± 66 pg/ml, $P = 0.03$; 90 min = 254 ± 55 pg/ml, $P = 0.03$) compared to the RE-M trial (30 min = 412 ± 95 pg/ml; 90 min = 335 ± 65 pg/ml), but were not significantly different compared to the NoRE trial (30 min = 381 ± 78 pg/ml; 90 min = 310 ± 64 pg/ml, $P = 0.09$). At 60 min after the meal, PP concentrations were $\sim 22\%$ and $\sim 34\%$ lower during the M-RE trial (246 ± 52 pg/ml) compared to the NoRE (315 ± 68 pg/ml, $P = 0.04$) and RE-M (375 ± 84 pg/ml, $P < 0.01$) trial, respectively. These data suggest that RE reduces PP concentrations in both the fasted state prior to a meal and in the postprandial state.

Discussion

Proper control of appetite and satiety plays a crucial role in weight loss and weight maintenance. This is the first study to compare how pre and postmeal RE impacts appetite and satiety regulation in adults with type 2 diabetes. Partially supporting our original

hypothesis, premeal RE reduced perceived hunger and increased perceived fullness prior to the meal, an effect that was associated with reduced acylated ghrelin concentrations. Furthermore, both pre and postmeal RE reduced postprandial perceived hunger, whereas only postmeal RE increased postprandial perceived fullness. Neither pre nor postprandial PYY concentrations were affected by RE timing. Both pre and postprandial PP concentrations were reduced during RE, and at the cessation of RE, PP concentrations rebounded to concentrations that were similar to no exercise. Taken together, both pre and postmeal RE have beneficial effects on the perception of appetite and satiety (i.e. moves perceived appetite and satiety in a direction that would reduce or limit food intake), and thus may aid in weight loss or maintenance efforts in individuals with type 2 diabetes.

The effect of acute RE on appetite and satiety is not consistent across all studies. Some studies in non-diabetic individuals show that acute RE lowers perceived hunger (6), and this coincides with reduced acylated ghrelin concentrations (6) (an effect expected to reduce perceived hunger) and increases in PP concentrations (2) (an effect expected to increase perceived fullness and reduce hunger). This acute “exercise anorexia” is short lived and dissipated after RE was stopped, and did not alter postprandial perceived hunger, acylated ghrelin, PYY (6), or energy intake at a subsequent buffet meal (2) compared to a no exercise trial. Yet, another study reported that acute RE did not alter perceived hunger immediately after RE, but 30 min later resulted in an 18% increase in *ad libitum* energy intake in non-diabetic individuals (19). Further, another report noted that an acute session of circuit RE increased acylated ghrelin concentrations after exercise (an effect that would be expected to increase energy intake) (24). The present data adds to this mix of findings in non-diabetic individuals and shows for the first time that an acute RE session prior to dinner reduces perceived hunger and acylated ghrelin concentrations, while increasing perceived fullness in individuals with type 2 diabetes. In this context, the mechanism for reduced acylated ghrelin concentrations may have been mediated by reduced stomach and intestinal blood flow during RE (22), which may have reduced the amount of ghrelin that was acylated by the gut enzyme ghrelin O-acyltransferase (25). In addition, an increase in vagal nerve activity decreases ghrelin secretion into circulation (1). Thus, it is possible that with premeal RE, vagal nerve activity increased which resulted in reduced ghrelin secretion from the stomach. In regards to perceived fullness in the current study, reduced perceived fullness prior to dinner with RE was not associated with higher PP concentrations, but instead with reduced PP concentrations (an effect that would be expected to increase perceived fullness). This finding contrasts another study in non-diabetic individuals, where PP concentrations increased after RE in the fasting state (2). The reason for this discrepant finding may be that individuals with type 2 diabetes have impaired PP responses to RE compared to healthy, non-diabetic individuals. Another possibility is that differences in study designs including time of day of testing (afternoon vs. evening), intensity of RE, and frequency and timing of blood sampling might explain these discrepancies.

A novel aspect of this study is that perceived appetite and satiety were examined with RE performed after dinner. Prior to this study, only one study had examined how exercise timing alters perceived appetite and satiety (9). In non-diabetic young men, 50 min of cycling exercise (60% $\text{VO}_{2\text{max}}$) starting 2 h after a breakfast meal resulted in lower

postprandial perceived hunger and greater postprandial PYY concentrations compared to not exercising (9). This study suggested that postmeal aerobic exercise extends the appetite suppressing effect of a meal, and in accord with this finding, our investigation also shows that postmeal RE extends the appetite suppressing effect of a dinner meal in adults with type 2 diabetes. The extension of suppressed perceived appetite in our study was not associated with increased postprandial PP or PYY concentrations (a response that would be expected to increase perceived fullness). Instead, we found that postmeal RE reduced postprandial PP concentrations (an effect expected to reduce perceived fullness and increase hunger) during the exercise period, but once exercise was stopped, PP concentrations rebounded to concentrations that were similar to the other trials. The mechanism for this response is not completely understood, but it is possible that RE during this time after a meal inhibits PP secretion from the gamma cells of the pancreas, even in the face of an increase in vagal nerve activity. Before the meal and during the time frame when PP concentrations were reduced with RE (~ -35 min prior to the meal), perceived fullness was higher. During the postprandial period when RE was performed (~45-90 min after the meal), PP concentrations were also reduced, but this was not associated with changes in perceived fullness at these specific times. It was not until 3.5 – 4 h after the meal that the appetite suppressing effect of postmeal RE emerged. This disconnect between acylated ghrelin, PP, and PYY with perceived appetite and satiety suggests that the regulation of appetite is complex and that other factors (i.e. hormones, substrates, or neural) contribute to RE induced alterations in appetite and satiety.

This study has some limitations that should be acknowledged. We did not assess food intake under free living conditions and instead we used a fixed size meal, thus it is not known if the observed changes in perceived hunger and fullness would directly translate into altered eating behavior in a real world setting. The standardized meal was used to control for the effect that meal size could have on perceived hunger, fullness, and hormonal responses. The RE session performed was, based on RPE, more of a moderate intensity exercise session, thus it is not known how other exercise intensities may alter perceived appetite, satiety, or hormonal responses. Another limitation is that the subjects in this study were taking diabetes medications that could potentially alter perceived appetite and satiety. To control for this unknown we used a within-subject repeated measures design study so that each condition was tested on the same person taking the same medication. Having the subjects take their medications as prescribed by their physician makes these findings more translational to the real world setting. Additionally, it is often questioned whether total AUC or *i*AUC should be reported. Since we studied the hormone responses over multiple study days and adults with type 2 diabetes are known to have considerable variability in their hormone concentrations, we opted to report *i*AUC values to minimize the effect of any day to day variability in the fasting hormone concentrations. Lastly, there is evidence that sex may influence the effect of exercise on appetite and satiety (12), and although the present study used both men and women, the sample size is not adequate to investigate sex differences.

In summary, both pre and postmeal RE alter perceived appetite and satiety in different manners. Premeal RE decreased premeal perceived hunger, acylated ghrelin, and PP concentrations, and also decreased postprandial perceived hunger. Further, premeal RE

increased perceived fullness prior to the meal, but did not alter postprandial perceived fullness. Postmeal RE reduced postprandial perceived hunger and PP concentrations, and resulted in an increase in postprandial perceived fullness, thus extending the appetite and satiety effect of dinner. Taken together, both exercise times reduced perceived hunger and increased perceived fullness, and these effects would be expected to reduce or help control food intake and aid in weight loss or maintenance efforts in individuals with type 2 diabetes.

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Figure 1.

Experimental timeline during each testing period

NoRE = no resistance exercise trial, RE-M = premeal resistance exercise trial, M-RE = postmeal resistance exercise trial, CGM = continuous glucose monitor.

Figure 2.

Perceived appetite and satiety ratings during testing

A) Perceived hunger time course, B) Premeal perceived hunger *iAUC*, C) Postprandial perceived hunger *iAUC*, D) Perceived fullness time course, E) Premeal perceived fullness *iAUC*, and F) Postprandial perceived fullness *iAUC*.

NoRE = no resistance exercise trial, RE-M = premeal resistance exercise trial, M-RE = postmeal resistance exercise trial. In Figure A and D, the underlined RE-M or M-RE corresponds to the time frame when exercise was performed during the trial.

Symbols by error bar indicate significant differences for individual time points.

RE-M significantly lower compared to NoRE ($P < 0.01$) and M-RE ($P = 0.01$).

M-RE significantly lower compared to NoRE ($P = 0.03$).

** RE-M significantly lower compared to NoRE ($P = 0.03$).

* RE-M significantly greater compared to NoRE ($P = 0.03$).

\$ M-RE significantly greater compared to NoRE ($P = 0.03$).

\$\$ M-RE significantly greater compared to NoRE ($P = 0.002$) and RE-M ($P = 0.03$).

All values are means $\pm$ S.E.M.

Figure 3.

Acylated ghrelin, pancreatic polypeptide, and peptide YY concentrations during testing.

A) Acylated ghrelin time course, B) Premeal acylated ghrelin *iAUC*, C) Postmeal acylated ghrelin *iAUC*, D) Pancreatic polypeptide time course, E) Premeal pancreatic polypeptide *iAUC*, F) Postmeal pancreatic polypeptide *iAUC*, G) Peptide YY time course, H) Premeal peptide YY *iAUC*, I) Postmeal peptide YY *iAUC*.

NoRE = no resistance exercise trial, RE-M = premeal resistance exercise trial, M-RE = postmeal resistance exercise trial. In Figure A, D, and G the underlined RE-M or M-RE corresponds to the time frame when exercise was performed during the trial.

Symbols by error bar indicate significant differences for individual time points.

RE-M significantly lower compared to NoRE ($P < 0.01$) and M-RE ($P < 0.01$).

* NoRE significantly different compared to M-RE ($P < 0.01$) and RE-M ($P < 0.01$).

\$ M-RE significantly different compared to NoRE ($P = 0.04$) and RE-M ($P < 0.01$).

RE-M significantly lower compared to M-RE ($P = 0.01$).

** NoRE significantly greater compared to RE-M ($P < 0.01$) and M-RE ($P < 0.01$).

\$\$ M-RE significantly lower compared to RE-M ($P = 0.03$).

All values are means $\pm$ S.E.M.

Table 1**Participant Characteristics and Medication Use**

Characteristics	
Age (y)	47 ± 12
Height (m)	1.68 ± 0.11
Weight (kg)	103.8 ± 23.7
Body mass index (kg/m ²)	36.5 ± 5.5
Body Fat (%)	39.0 ± 8.7
Fasting Glucose (mmol/l)	8.16 ± 2.44
Hemoglobin A1C % (% [mmol/mol])	7.2 ± 1.1 [55.2]
Medication Usage	
No Medications	1 Participant
Metformin Only	2 Participants
Metformin, Glyburide	1 Participants
Metformin, Fenofibrate	1 Participant
Metformin, Lipitor	1 Participant
Metformin, Januvia	2 Participants
Metformin, Pravastatin	1 Participant
Metformin, Lisinopril, Pravastatin	1 Participant
Glimepiride, Pravastatin, Lisinopril	1 Participant
Janumet, Glyburide, Lisinopril, Lyrica	1 Participant

Values are means ± S.D.

5 M / 7 F

Table 2

Metabolic data and rating of perceived exertion (RPE) during each resistance exercise session.

	RE-M	M-RE
Duration (min)	45 ± 1	47 ± 2
Oxygen consumption (ml kg ⁻¹ min ⁻¹)	6.1 ± 0.4	6.1 ± 0.3
Energy Expenditure (Gross kcal)	140 ± 16	141 ± 15
Respiratory Exchange Ratio	1.00 ± 0.01	1.00 ± 0.01
Heart Rate (bpm)	105 ± 5	110 ± 5*
Average RPE (BORG 6-20 scale)	12 ± 1	12 ± 1

Values are means ± S.E.M.

RE-M = premeal resistance exercise, M-RE = postmeal resistance exercise.

For the variables time, oxygen consumption, energy expenditure, respiratory exchange ratio, and heart rate, only data for N = 11 is reported. For RPE, data for N = 12 is reported.

* P < 0.05 compared to heart rate during the RE-M trial.