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► **To cite this version:**

Tanya M. Halliday, Corey A. Rynders, Elizabeth Thomas, Audrey Bergouignan, Zhaoxing Pan, et al.. Appetite-Related Responses to Overfeeding and Longitudinal Weight Change in Obesity-Prone and Obesity-Resistant Adults. *Obesity*, 2020, 28 (2), pp.259-267. 10.1002/oby.22687 . hal-02868542

HAL Id: hal-02868542

<https://hal.science/hal-02868542v1>

Submitted on 22 Aug 2024

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Published in final edited form as:

Obesity (Silver Spring). 2020 February ; 28(2): 259–267. doi:10.1002/oby.22687.

Appetite-related responses to overfeeding and longitudinal weight change in obesity prone and obesity resistance adults

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Abstract

Objective: Appetite responses to 3-d of overfeeding (OF) were examined as correlates of longitudinal weight change in adults classified as obesity-prone (OP) or obesity-resistant (OR).

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Author contributions: TH CAR and ET analyzed and interpreted the data and wrote the first draft of the manuscript. PZ assisted with data analysis and interpretation. AB assisted in the interpretation of the data and writing. EK carried out the experiments. MC and DB conceived and carried out the experiments, interpreted the data, and edited the final draft of the manuscript. All authors were involved in writing the paper and had final approval of the submitted and published versions.

[ClinicalTrials.gov](https://clinicaltrials.gov) Identifier:

Disclosure: No conflict of interest to declare.

Methods: OP (n=22) and OR (n=30) adults consumed a controlled eucaloric (EU) and OF diet (140% energy needs) for 3-days followed by 3-days of *ad libitum* feeding. Hunger and satiety were evaluated by visual analog scales. Ghrelin and PYY were measured during a 24-hr inpatient visit on day 3. Body weight and composition were measured annually for 4.0 ± 1.3 years.

Results: Dietary restraint and disinhibition were greater in OP than OR (mean difference: 3.5 ± 1.2 and 3.3 ± 0.9 , respectively $p < 0.01$) participants and disinhibition was associated with longitudinal weight change (n=48; $r = 0.35$; $p = 0.02$). Compared to the EU diet, EI fell significantly in OR subjects following OF ($p = 0.03$) but not in OP ($p = 0.33$). 24 h PYY area under the curve increased with OF in OR ($p = 0.02$) but not OP ($p = 0.17$). Furthermore, changes in PYY with OF correlated with measured EI ($r = -0.36$, $P = 0.01$).

Conclusions: Baseline disinhibition and PYY responses to OF differed between OP and OR adults. Dietary disinhibition was associated with 5-year longitudinal weight gain. Differences in appetite regulation may underlie differences in propensity for weight gain.

Keywords

Hunger; satiety; ghrelin; PYY; overfeeding; obesity

INTRODUCTION:

The prevalence of obesity has increased over a relatively short period¹. The modern obesogenic environment is likely a contributing factor^{2,3}. Periods of excessive energy intake (EI) with or without reductions in physical activity leading to repeated periods of positive energy balance and weight gain have become 'normal'.

Interestingly, despite living in the same environment, approximately one-third of Americans maintain a normal body weight. Understanding physiological and behavioral mechanisms that differ between obesity prone (OP) and obesity resistant (OR) individuals could provide valuable information on novel strategies to manage or prevent overweight/obesity. Our Energy Adaptations over Time Study (EATS) compared OP and OR adults classified by family and personal weight history and found that differences in substrate oxidation⁵, neuronal responses to visual food cues^{6,7}, dietary restraint and disinhibition⁸, and free-living physical activity following brief periods of overfeeding⁹ may explain a propensity for weight gain.

The present analysis compares appetite-related hormones [ghrelin and peptide YY (PYY)], subjective appetite, and *ad libitum* EI following 3-d of overfeeding (OF) versus 3-d of eucaloric intake (EU) in OP and OR adults. . An additional aim was to determine whether acute responses to OF were associated with longitudinal weight change over 5-yrs of follow-up.

MATERIALS AND METHODS:

Participants

Characteristics of this cohort have been previously described^{5,10}. Non-obese (BMI < 30 kg/m²), weight-stable ($\pm 5\%$ for 3 months), young (25-35 years), men and women classified

as OR or OP were eligible for enrollment. OR participants defined themselves as “constitutionally thin”, not needing to exert effort to maintain their weight, and having no 1st degree relatives with a BMI >30 kg/m². OP participants identified themselves as having to exert conscious effort to maintain their weight and reported at least one 1st degree relative with a BMI >30 kg/m². The Colorado Multiple Institutional Review Board approved the study protocol. Participants provided written informed consent prior to participation.

Study Design

Detailed information on the design has previously been published^{5,9,11}. Briefly, each participant completed baseline evaluations including: height, weight, body composition via dual energy x-ray absorptiometry (DEXA; Hologic Discovery W, Bedford, MA); Three Factor Eating Inventory Questionnaire (TFEQ)¹² and Power of Food Scale (PFS)¹³. Each participant then completed two 10d controlled-feeding study phases in a randomized, cross-over, counterbalanced design, separated by at least 1 month. Each 10d study phase consisted of 1) an outpatient 4d eucaloric (EU) run-in diet (Study Days 1-4), 2) a 3d EU or OF (40% above estimated energy needs) diet period (Study Days 5-7, of which days 5 and 6 were outpatient and day 7 was inpatient), and 3) an outpatient 3d *ad libitum* feeding period, during which food intake was directly measured (Supplementary Figure, S1). Participants were invited to return for repeat DXA scans annually for 5yr. Participants completing 1 yr of follow-up are included in the present analysis.

Run-In Diet: To ensure energy and macronutrient balance, participants consumed a controlled EU diet (20% protein, 34% fat, 46% carbohydrate) for 4d at the start of each study phase. The caloric value of the diet was individualized for each participant and determined using measured resting metabolic rate and fat-free mass. Basal energy needs were multiplied by an activity factor of 1.4 – 1.65, based upon 7d of activity monitoring (pedometer). All food was prepared by the Colorado Clinical and Translational Research Center (CTRC)’s metabolic kitchen. Participants consumed breakfast on the unit each day, and the remainder of the meals were packaged for them to take with them. Participants were instructed to consume only the food provided, and were queried on adherence the following day.

Study Diets and Inpatient Stay: Following the 4d EU run-in, participants consumed a controlled EU or OF diet (140% of baseline energy needs) in a randomized order for 3 subsequent days (Study days 5-7). Macronutrient content was the same as the run-in diet. All food was prepared by the CTRC metabolic kitchen. Participants consumed breakfast on the unit each day, and the remainder of the meals were packaged for them to take with them. Participants were instructed to consume only the food provided, and were queried on adherence the following day. On the third day of the study diet (Study Day 7) participants were admitted to the inpatient CTRC at 0700 in the fasting state for a 24hr stay in a metabolic chamber. Breakfast, lunch, dinner, and a snack were provided at 0730 (25% daily EI based on the EU or OF diet), 1200 (30% daily EI), 1700 (30% daily EI), and 2000 (15% daily EI), respectively.

Ad Libitum Diet: Following the 24hr metabolic chamber stay, participants completed a 3d, free-living, *ad libitum* feeding period (Study Days 8-10) using weigh and measure techniques to monitor EI. The amount of food offered to participants during the *ad libitum* portion was 125% of baseline energy needs. Participants were instructed to eat as much food as desired, and to return unconsumed food. Breakfast was consumed on the unit each day, and the remainder of the meals were packaged for participants to take with them. All food for the 10d study period was provided by the CTRC metabolic kitchen.

Measurements:

Appetite Ratings: Immediately before and after each meal during the 3-d study diet phase (Study days 5-7) and the subsequent 3d *ad libitum* EI phase (Study Days 8-10), participants rated hunger, satiety, and prospective food consumption (PFC) using 100mm visual analogue scales (VAS) on a personal digital assistant¹⁴.

Appetite-Related Hormonal Analysis: At the start of the inpatient metabolic chamber stay (Day 7), an intravenous catheter was inserted in the antecubital vein for blood sampling. Blood was drawn in the fasted state for ghrelin and PYY. Following breakfast, blood was sampled at 0830 and again every 30 minutes for 210 minutes, then at clock times 1300, 1500, 1700, 1800, 2000, and then again at 0200 and 0700 the following day (Day 8). The day 8 0700 blood was also analyzed for leptin. Radioimmunoassays were used to measure leptin (Millipore), PYY (Millipore), and total ghrelin (Millipore) by the CTRC Core Laboratory.

Statistical Analyses

Data were analyzed using SAS version 9.4 (SAS Institute, Inc., Cary, NC, USA). A P-value <0.05 was considered statistically significant. All data are presented as mean \pm standard error. VAS data were summarized as the daily average over the 3d study diet phase (Days 5-7) and over the 3d *ad libitum* intake phase (Days 8-10). Hormone data obtained on day 7 were summarized as the incremental area under the curve (iAUC) above or below baseline. iAUC was calculated using trapezoidal reconstruction for the entire 24-hr. chamber stay as well as for the daytime (0800-2200), nighttime (2200-0600), breakfast, lunch, and dinner (plus snack) periods separately. All outcomes were analyzed using separate linear mixed models (LMM) models (SAS PROC MIXED procedure). Each LMM consisted of group (OP, OR), diet (EU, OF), sequence (order of diet consumption), period (visit in which the diets were consumed), and interaction of group and diet as fixed effects and participants as random effects. Pearson correlation analysis was conducted among mean changes (response=overfed-eucaloric condition) in *ad libitum* intake (Days 8-10), mean changes in VAS scores (hunger, PFC, and satiety), mean changes in hormones (ghrelin, PYY, and leptin), and baseline self-report eating behavior scores (TFEQ and PFS). Mean changes in VAS scores, self-report eating behavior scores, and hormones were also explored as correlates of longitudinal body weight and composition changes. The longitudinal data were expressed as rate of body weight change (RoWC) and rate of fat mass change (RoFMC) calculated as the difference between the last follow-up time point minus baseline divided by the number of follow-up years.

Results

Study Participants

Fifty-two participants (22 OP, 30 OR) completed both EU and OF study periods. N=4 participants (2 OP, 2 OR) were omitted from the hormone analyses due to invalid plasma data. Correlational analyses were performed on individuals with valid data for both feeding conditions and 1 year of follow-up data (n=48; 22 OP, 26 OR). Participant characteristics are presented in Table 1. OP had a higher weight, BMI and fat mass than OR. At baseline OP participants reported greater levels of dietary restraint and disinhibition on the TFEQ, and higher PFS scores than the OR group (Table 1). Group differences in dietary restraint and disinhibition remained after statistical adjustment for BMI.

Ad libitum EI

Figure 1 displays changes in energy and macronutrient intake (OF-EU) during the study diet phase (Days 5-7) and each day of the *ad libitum* diet phases (Days 8-10). Average EI over the 3d *ad libitum* period was not different between groups (diet x group interaction, $p=0.50$). However, when OP and OR were examined independently, the within-group decrease in EI following overfeeding relative to the eucaloric diet was significant in OR (-181.8 ± 82.8 kcal, $P=0.03$), whereas the within-group decrease in EI was not significant in the OP (-114.3 ± 81.9 kcal, $P=0.33$). The largest decrease in EI for both groups occurred on day 8, immediately after the period of imposed OF.

Hunger, PFC, and Satiety

VAS measures summarized by day and as averages over each study phase are shown in Figure 2. OF decreased pre-meal hunger and PFC and increased post-meal satiety similarly in both groups during days 5-7 (P -values < 0.004). Following OF (*ad libitum* phase), VAS ratings of hunger, PFC, and satiety were similar to ratings given during the EU condition (P -values > 0.05). Meal-specific (i.e. breakfast, lunch, and dinner + snack) appetite ratings during the first day of controlled feeding (EU or OF) and on the first day of the *ad libitum* period did not differ between groups (Supplemental Figure S2)

24-hr Ghrelin and PYY, and Fasting Leptin

Figure 3 depicts ghrelin and PYY concentrations over 24h during the inpatient visits. iAUC values (24hr, day, night, and per meal) are shown in Figure 4. Mean ghrelin iAUC over 24hr was $-11.3 \pm 1.2\%$ lower in OP and $-6.2 \pm 1.6\%$ lower in OR following OF, but the group x diet interaction was not significant ($P=0.91$). Post-meal suppression of ghrelin during the daytime was also not different between groups (diet x group interaction, $P=0.84$).

Over 24hr, PYY iAUC was $75 \pm 9.4\%$ higher during OF in OR ($p=0.02$) and $41.1 \pm 7.6\%$ higher in OP with no difference between groups (diet x group interaction, $P=0.39$). However, when OP and OR were examined independently, the within-group increase in PYY during OF was significant in the OR group ($P=0.02$), but not in the OP ($P=0.17$). There were also trends for significant between group differences for the PYY responses to breakfast (diet x group interaction, $P=0.05$) and dinner (diet x group interaction, $P=0.09$). During overfeeding the OP group had an increase in PYY relative to the EU condition whereas PYY was not

different between conditions in the OR at breakfast. In contrast, the PYY response to dinner was increased relative to EU feeding in OR but not in OP. The trends for between group differences in PYY at breakfast and dinner remained after statistical adjustment for BMI.

Fasting leptin concentrations were higher in OP compared to OR under both experimental conditions (P-value for group <0.001), but these differences disappeared after adjusting for fat mass (P-value for group= 0.61, supplemental figure, S3). Fasting leptin concentrations during OF were not significantly different from EU conditions in either group (P-value for diet effect=0.13).

Correlates of Ad Libitum EI and Prospective Weight Change

Bivariate correlations among baseline TFEQ, hormone and VAS responses to OF, and *ad libitum* EI are shown in Table 2. Scatter plots showing significant associations are presented in Figure 5. Individuals with higher TFEQ hunger ratings at baseline consumed more energy during the *ad libitum* period following the OF condition (Table 2, Figure 5). Similarly, individuals reporting increased hunger and PFC during OF consumed the most energy during the *ad libitum* diet. A greater increase in the PYY response to OF was associated with lower *ad libitum* intake during the subsequent 3d ($r=-0.36$, $P=0.01$, Table 2, Figure 5).

The OP and OR groups gained 3.5 ± 0.8 kg and 2.6 ± 0.6 kg of body weight, respectively with no differences between groups over 4.0 ± 1.4 year of follow-up ($P=0.70$). These changes in body weight corresponded to a 2.4 ± 0.7 kg increase in FM in OP and 1.9 ± 0.4 kg increase in FM in OR during the follow-up period. Bivariate correlations between the hormone responses to OF and prospective weight changes are shown in Table 3. None of the responses to OF explored were significant predictors of body weight or composition changes over the follow-up period. Higher TFEQ disinhibition ratings at baseline were associated with a greater rate of weight change (RoWC) that tended to be driven by OP (correlation coefficient for the combined group=0.35, $P=0.02$; correlation coefficient for OP=0.39, $P=0.12$; correlation coefficient for OR=0.11, $P=0.61$; Table 3, Figure 5).

DISCUSSION:

This study examined appetite-related hormonal and behavioral responses to short-term OF in adults classified as OP and OR and tested whether acute responses were associated with long-term weight gain. Findings indicate differences in some of these variables between OP and OR individuals which may be involved in the propensity for weight gain. Specifically, in response to OF, within-group 24h PYY values were significantly increased in the OR, but not the OP group, and average EI for the 3d *ad libitum* feeding period was significantly reduced in OR, but not OP subjects. In addition, while OP and OR adults gained similar amounts of body mass over 5yrs of follow-up, higher baseline dietary disinhibition was associated with greater RoWC, an effect that was driven primarily by the OP group.

Consistent with our previous study⁸, we found OP adults demonstrate greater dietary restraint and disinhibition¹², as well as a greater drive to consume palatable foods in the absence of physiological hunger¹³. Disinhibition and hedonic hunger have been positively correlated with obesity and weight gain¹⁵⁻¹⁹ in other studies. The relationship between

data are consistent with the idea that OP individuals may be more susceptible to reduced satiety and greater EI during the evening. Evidence has consistently shown an association between EI later in the day with increased BMI³⁰.

Our group previously reported no differences in fasting nor postprandial PYY responses to 1d of OF between OP and OR adults, as well as no overall diet effect of OF on PYY levels¹⁴. Though, interestingly in that prior study, underfeeding did result in a significant reduction in PYY¹⁴. It is possible that the degree of OF in our trials was not great enough to elicit significant changes in PYY levels. Other investigators reported an increase in fasting PYY levels following 7d of OF at 170% of energy needs in men³¹. Furthermore, the increase in fasting PYY levels in that trial were not related to adiposity status³¹, which is in agreement with our finding that PYY levels do not differ between OP and OR phenotypes. Of note, a small ‘free-living’ 4wk OF intervention comparing women with constitutional thinness (BMIs similar to anorexia nervosa patients, but without an eating disorder) and normal weight controls found that constitutionally thin participants demonstrated an increase in post-prandial PYY following OF while the normal weight controls experienced a decrease in post-prandial PYY³². Thus, in rare cases of extreme obesity resistance, gut peptides may play a role in the preservation of a thin phenotype. In our OR subjects reporting not having to exert effort to maintain a normal BMI, gut peptides appear to be of less importance. Furthermore, the PYY response to short-term OF was not associated with longitudinal weight change, further suggesting that this gut hormone may not be predictive of long-term weight gain.

Contrary to our hypothesis, ghrelin was not influenced by OF in either group. This is surprising, as we expected OF to decrease ghrelin concentrations and thus promote a reduction in subsequent EI. Inconsistent findings in ghrelin responses to OF exist in the literature. We previously found a reduction of postprandial ghrelin iAUC in response to 1d of OF in OP and OR adults¹⁴ and Robertson et al. demonstrate greater post-prandial ghrelin suppression in response to an oral fat tolerance test after 3 wks of high fat feeding in a small (n=6) study of healthy males³³. Other investigations have also demonstrated no change in fasting or post-OGTT ghrelin following short-term (3d) OF^{34,35}. Though, fasting acylated ghrelin has been shown to increase following short-term overfeeding³³, further complicating our understanding of ghrelin’s role in maintaining energy balance. Discrepant outcomes are likely related to different OF protocols, form of ghrelin (acylated vs de-acylated vs total) measured, and health-status of participants. In addition to ghrelin’s appetite-specific roles, it is also implicated in glucose regulation and thus responses to short-term OF could be more related to glycemic control than appetite regulation^{36,37}.

Based on prior findings from our group and others, we hypothesized that RoWC would be greater in OP vs OR adults. With five years of follow-up, no statistically significant difference in RoWC nor body composition were detected between these groups. However, it is important to note that the OR group entered the study with lower BMIs, and therefore maintained a lower BMI through follow-up. This could have important implications for cardiometabolic health outcomes and weight gain trajectories beyond our follow-up period. While no differences in RoWC between the groups was apparent, baseline disinhibition was positively associated with RoWC, an effect driven by the OP group. Our findings add

information on how dietary constructs prospectively influence weight gain and extends prior retrospective analyses. Specifically, Hays and Roberts previously reported that higher levels of disinhibition were associated with ~22 kg of weight gain over a 20 yr period³⁸. This trial enrolled older women and asked them to self-report their body mass at 6 prior age ranges. Interestingly, they evaluated subscales of the TFEQ and found that ‘habitual disinhibition’ which is the susceptibility to overeat in response to daily life circumstances (e.g. – nearly constant access to energy dense, palatable foods) was the greatest predictor of weight gain. Collectively, these data indicate that easy-to-administer questionnaires may provide valuable insight on risk of future weight gain. Furthermore, targeting disinhibition could be an effective intervention approach.

We acknowledge a number of limitations to this study. First, OP and OR phenotypes are based on self-report, and these groups differed in body mass and composition at study onset. Second, measurements of appetite ratings occurred only before and after meals, and do not overlay on the blood sampling time points during the inpatient stay. Third, blood sampling occurred most frequently following the breakfast meal on Day 8 and was not conducted at uniform times following each meal. Similarly, the night-time blood sampling period has only 2 collections, in order to avoid disrupting participants’ sleep. Fourth, we measured total forms of ghrelin and PYY and therefore are unable to comment on how the active forms of these hormones may be altered. Fifth, we acknowledge that the significant increase in 24hr PYY and decrease in 3d *ad libitum* EI following OF in the OR group vs. no significant changes in the OP group, is not synonymous with between-group differences and may represent a difference in nominal significance³⁹. Thus, we cautiously present these findings. However it is important to note that the trial was not powered to detect significant group by time interactions in this secondary analysis. Finally, we had a reduced sample size for the longitudinal weight change analysis which could have reduced our ability to detect significant relationships.

CONCLUSIONS:

Our data indicate OP adults exhibit greater dietary disinhibition than OR adults, and greater baseline disinhibition was associated with greater weight gain over 5 yrs of follow-up. Furthermore, OF resulted in significant increases in PYY iAUC and reductions in 3d *ad libitum* EI in the OR group, but not the OP group, providing information on potential physiological differences in these phenotypes. However, no difference in longitudinal weight gain occurred between these groups. Trials with larger samples for longitudinal follow-up and examination of other behavioral and physiological predictors of weight change will be required to confirm these relationships and determine if OP and OR classifications are predictive of weight gain.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS:

We acknowledge and thank the University of Colorado Clinical and Translational Research Center (CTRC) staff. **Data Sharing:** Deidentified data will be available beginning 3 months and ending 5 years following article publication to researchers who provide a methodologically sound proposal. Direct proposals to Daniel.bessesen@cuanschutz.edu.

Funding: This research was supported by the NIH/NIDDK Colorado Nutrition Obesity Research Center (5 P30 DK048520-21), NIH/National Center for Research Resources Colorado Clinical and Translational Sciences Institute Grant (UL 1 RR025780), K01 DK113063 (CAR), R00DK100465 (AB), K24 DK02935 (DHB), RO1 DK62874 (DHB), T32 DK07658 (TMH). The funders had no role in study design, data collection and analysis, the decision to publish, or preparation of the manuscript.

REFERENCES:

1. Flegal KM, Kruszon-Moran D, Carroll MD, Fryar CD, Ogden CL. Trends in obesity among adults in the united states, 2005 to 2014. *JAMA*. 2016;315(21):2284–2291. [PubMed: 27272580]
2. Mattes R, Foster GD. Food environment and obesity. *Obesity (Silver Spring, Md)*. 2014;22(12):2459–2461.
3. Wadden TA, Brownell KD, Foster GD. Obesity: responding to the global epidemic. *Journal of consulting and clinical psychology*. 2002;70(3):510–525. [PubMed: 12090366]
4. Bulik CM, Allison DB. The genetic epidemiology of thinness. *Obesity reviews : an official journal of the International Association for the Study of Obesity*. 2001;2(2):107–115. [PubMed: 12119662]
5. Schmidt SL, Kealey EH, Horton TJ, VonKaenel S, Bessesen DH. The effects of short-term overfeeding on energy expenditure and nutrient oxidation in obesity-prone and obesity-resistant individuals. *International journal of obesity (2005)*. 2013;37(9):1192–119 [PubMed: 23229737]
6. Cornier MA, McFadden KL, Thomas EA, Bechtell JL, Bessesen DH, Tregellas JR. Propensity to obesity impacts the neuronal response to energy imbalance. *Frontiers in behavioral neuroscience*. 2015;9:52. [PubMed: 25767441]
7. Cornier MA, McFadden KL, Thomas EA, et al. Differences in the neuronal response to food in obesity-resistant as compared to obesity-prone individuals. *Physiology & behavior*. 2013;110-111:122–128. [PubMed: 23313402]
8. Thomas EA, Bechtell JL, Vestal BE, et al. Eating-related behaviors and appetite during energy imbalance in obese-prone and obese-resistant individuals. *Appetite*. 2013;65:96–102. [PubMed: 23402714]
9. Creasy SA, Rynders CA, Bergouignan A, Kealey EH, Bessesen DH. Free-Living Responses in Energy Balance to Short-Term Overfeeding in Adults Differing in Propensity for Obesity. *Obesity (Silver Spring, Md)*. 2018;26(4):696–702.
10. Rynders CA, Pereira RI, Bergouignan A, Kealey EH, Bessesen DH. Associations Among Dietary Fat Oxidation Responses to Overfeeding and Weight Gain in Obesity-Prone and Resistant Adults. *Obesity (Silver Spring, Md)*. 2018;26(11):1758–1766.
11. Schmidt SL, Harmon KA, Sharp TA, Kealey EH, Bessesen DH. The effects of overfeeding on spontaneous physical activity in obesity prone and obesity resistant humans. *Obesity (Silver Spring, Md)*. 2012;20(11):2186–2193.
12. Stunkard AJ, Messick S. The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. *Journal of psychosomatic research*. 1985;29(1):71–83. [PubMed: 3981480]
13. Lowe MR, Butryn ML, Didie ER, et al. The Power of Food Scale. A new measure of the psychological influence of the food environment. *Appetite*. 2009;53(1):114–118. [PubMed: 19500623]
14. Thomas JLB EA, Bessesen DD, Tregellas JR, Cornier MA. Hormonal and Metabolic Effects of Short-term Energy Imbalance in Obese-Prone as Compared to Obese-Resistant Individuals. *Am J Diab Obes Met*. 2014;1(1):1–14.
15. Hays NP, Roberts SB. Aspects of eating behaviors “disinhibition” and “restraint” are related to weight gain and BMI in women. *Obesity (Silver Spring)*. 2008;16(1):52–58. [PubMed: 18223612]

16. Hays NP, Bathalon GP, McCrory MA, Roubenoff R, Lipman R, Roberts SB. Eating behavior correlates of adult weight gain and obesity in healthy women aged 55-65 y. *Am J Clin Nutr.* 2002;75(3):476-483. [PubMed: 11864852]
17. Drapeau V, Provencher V, Lemieux S, Despres JP, Bouchard C, Tremblay A. Do 6-y changes in eating behaviors predict changes in body weight? Results from the Quebec Family Study. *Int J Obes Relat Metab Disord.* 2003;27(7):808-814. [PubMed: 12821966]
18. Schultes B, Ernst B, Wilms B, Thurnheer M, Hallschmid M. Hedonic hunger is increased in severely obese patients and is reduced after gastric bypass surgery. *The American journal of clinical nutrition.* 2010;92(2):277-283. [PubMed: 20519559]
19. Carr KA, Lin H, Fletcher KD, Epstein LH. Food reinforcement, dietary disinhibition and weight gain in nonobese adults. *Obesity (Silver Spring, Md).* 2014;22(1):254-259.
20. Tuschl RJ, Platte P, Laessle RG, Stichler W, Pirke KM. Energy expenditure and everyday eating behavior in healthy young women. *Am J Clin Nutr.* 1990;52(1):81-86. [PubMed: 2360553]
21. Hill AJ, Weaver CF, Blundell JE. Food craving, dietary restraint and mood. *Appetite.* 1991 ;17(3): 187-197. [PubMed: 1799281]
22. Williamson DA, Lawson OJ, Brooks ER, et al. Association of body mass with dietary restraint and disinhibition. *Appetite.* 1995;25(1):31-41. [PubMed: 7495325]
23. Foster GD, Wadden TA, Swain RM, Stunkard AJ, Platte P, Vogt RA. The Eating Inventory in obese women: clinical correlates and relationship to weight loss. *Int J Obes Relat Metab Disord.* 1998;22(8):778-785. [PubMed: 9725638]
24. Urbanek JK, Metzgar CJ, Hsiao PY, Piehowski KE, Nickols-Richardson SM. Increase in cognitive eating restraint predicts weight loss and change in other anthropometric measurements in overweight/obese premenopausal women. *Appetite.* 2015;87:244-250. [PubMed: 25576021]
25. Lawson OJ, Williamson DA, Champagne CM, et al. The association of body weight, dietary intake, and energy expenditure with dietary restraint and disinhibition. *Obes Res.* 1995;3(2):153-161. [PubMed: 7719961]
26. Provencher V, Drapeau V, Tremblay A, Despres JP, Lemieux S. Eating behaviors and indexes of body composition in men and women from the Quebec family study. *Obes Res.* 2003;11(6):783-792. [PubMed: 12805400]
27. Bundrick SC, Thearle MS, Venti CA, Krakoff J, Votruba SB. Soda consumption during ad libitum food intake predicts weight change. *Journal of the Academy of Nutrition and Dietetics.* 2014;114(3):444-449. [PubMed: 24321742]
28. Stinson EJ, Piaggi P, Ibrahim M, Venti C, Krakoff J, Votruba SB. High Fat and Sugar Consumption During Ad Libitum Intake Predicts Weight Gain. *Obesity (Silver Spring, Md).* 2018;26(4):689-695.
29. Batterham RL, Cohen MA, Ellis SM, et al. Inhibition of food intake in obese subjects by peptide YY3-36. *The New England journal of medicine.* 2003;349(10):941-948. [PubMed: 12954742]
30. Beccuti G, Monagheddu C, Evangelista A, et al. Timing of food intake: Sounding the alarm about metabolic impairments? A systematic review. *Pharmacological research.* 2017;125(Pt B):132-141. [PubMed: 28928073]
31. Cahill F, Shea JL, Randell E, Vasdev S, Sun G. Serum peptide YY in response to short-term overfeeding in young men. *The American journal of clinical nutrition.* 2011;93(4):741-747. [PubMed: 21289220]
32. Germain N, Galusca B, Caron-Dorval D, et al. Specific appetite, energetic and metabolomics responses to fat overfeeding in resistant-to-bodyweight-gain constitutional thinness. *Nutrition & diabetes.* 2014;4:e126. [PubMed: 25027794]
33. Wadden D, Cahill F, Amini P, et al. Serum acylated ghrelin concentrations in response to shortterm overfeeding in normal weight, overweight, and obese men. *PLoS One.* 2012;7(9):e45748. [PubMed: 23029221]
34. Hagobian TA, Sharoff CG, Braun B. Effects of short-term exercise and energy surplus on hormones related to regulation of energy balance. *Metabolism.* 2008;57(3):393-398. [PubMed: 18249213]

35. Votruba SB, Kirchner H, Tschop M, Salbe AD, Krakoff J. Morning ghrelin concentrations are not affected by short-term overfeeding and do not predict ad libitum food intake in humans. *The American journal of clinical nutrition*. 2009;89(3):801–806. [PubMed: 19158212]
36. Heppner KM, Tong J. Mechanisms in endocrinology: regulation of glucose metabolism by the ghrelin system: multiple players and multiple actions. *European journal of endocrinology*. 2014;171(1):R21–32. [PubMed: 24714083]
37. Pöykkö SM, Kellokoski E, Hörkkö S, Kauma H, Kesäniemi YA, Ukkola O. Low Plasma Ghrelin Is Associated With Insulin Resistance, Hypertension, and the Prevalence of Type 2 Diabetes. *Diabetes*. 2003;52(10):2546. [PubMed: 14514639]
38. Hays NP, Roberts SB. Aspects of Eating Behaviors “Disinhibition” and “Restraint” Are Related to Weight Gain and BMI in Women. *Obesity (Silver Spring, Md)*. 2008;16(1):52–58.
39. Allison DB, Brown AW, George BJ, Kaiser KA. Reproducibility: A tragedy of errors. *Nature*. 2016;530(7588):27–29. [PubMed: 26842041]

Study Importance Questions:**What is already known?**

- Approximately 1/3rd of US adults maintain a normal body mass, despite living in an environment that promotes positive energy balance. Differences in the responses of appetite and energy intake following short periods of overfeeding (e.g., 3d) may explain why some individuals are prone to obesity while others seem to be resistant.

What does your study add?

- In this study we measured indices of appetite regulation in response to 3d of overfeeding (40% above usual intake) as compared to a eucaloric control condition in obesity-prone (OP) and obesity-resistant (OR) adult men and women.
- Our goal was to determine if appetite responses to 3d of overfeeding correlate with longitudinal weight gain.
- Appetite ratings and appetite-related hormonal responses to overfeeding were not different between adults classified as OP and OR, nor were these outcomes associated with longitudinal weight gain. However, dietary restraint and disinhibition were greater in OP compared to OR, and dietary disinhibition was associated with longitudinal weight gain in the combined group.

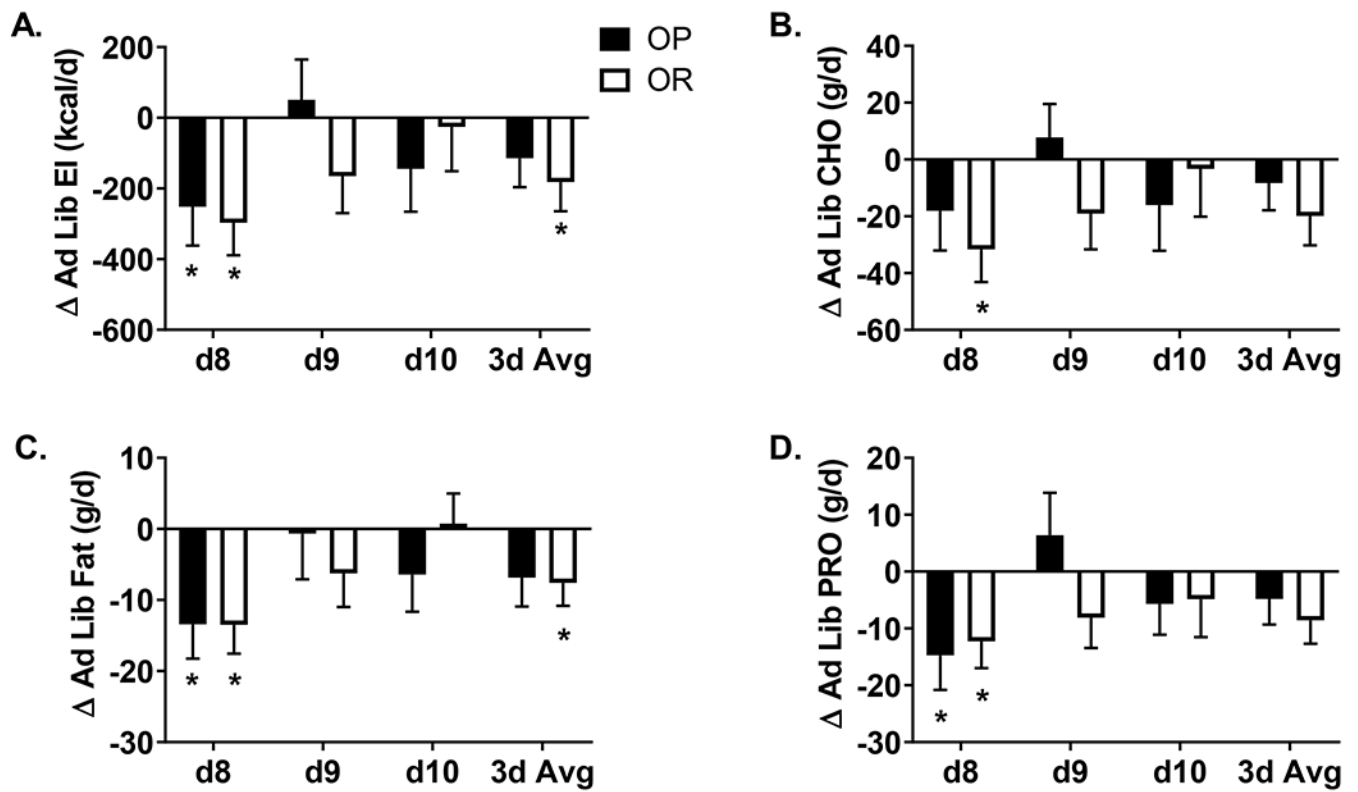


Figure 1.

Change in energy and macronutrient intake (OP-EU condition) for the study diet and *ad libitum* diet phases. Total energy intake (kcal) (A); Carbohydrate (g) (B), Fat (g) (C), and Protein (g) (D).

= overfed-eucaloric condition; EI: energy intake. * indicates significant within-group change in ad libitum intake following overfeeding vs. eucaloric feeding phases.

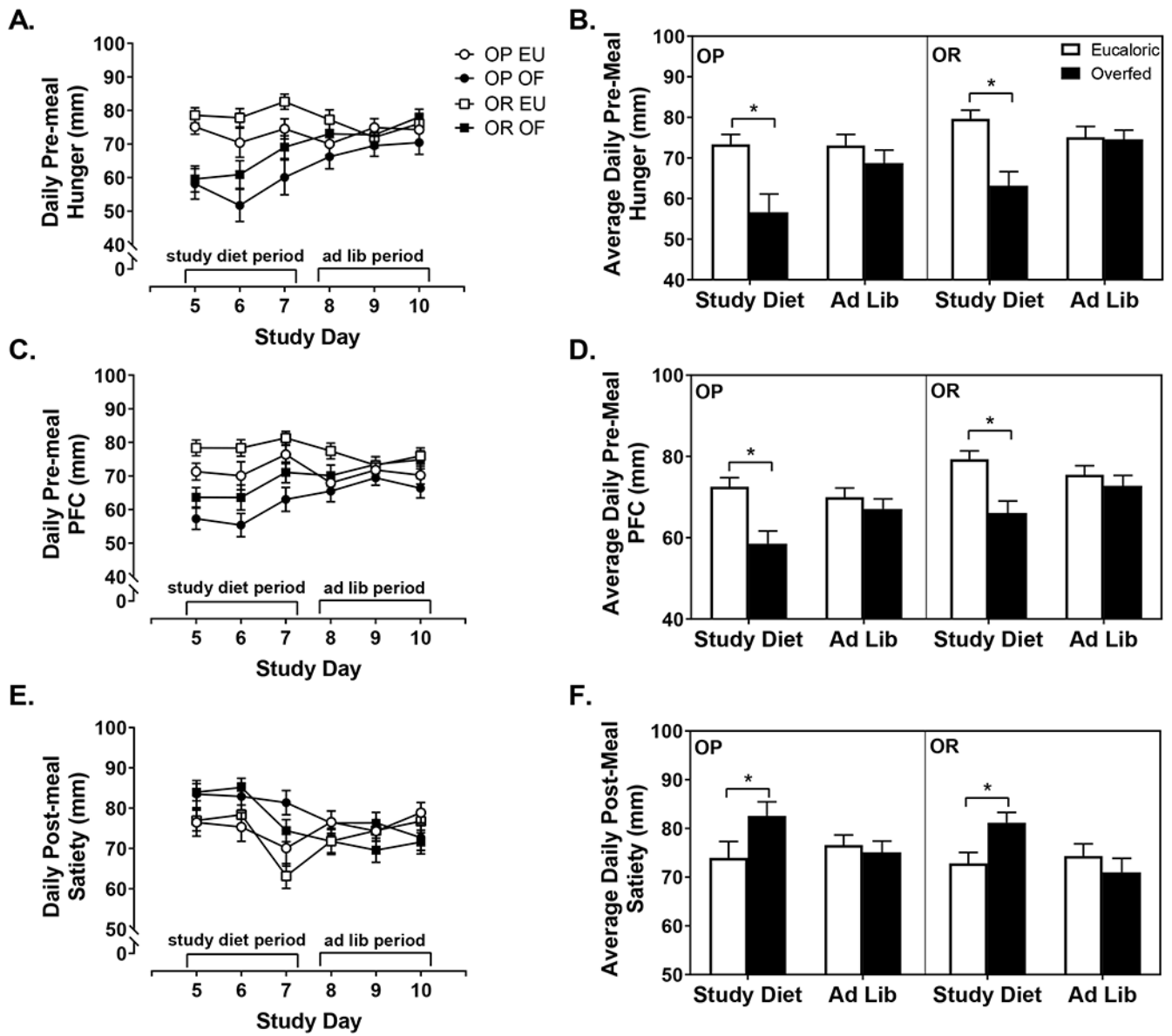


Figure 2.

Time course of visual analog scale measures of pre-meal hunger (A), pre-meal prospective food consumption (C), and post-meal satiety (E) in obesity prone (OP) and obesity resistant (OR) adults studied for 3d under controlled eucaloric (EU) and overfeeding (OF) conditions followed by a 3d *ad libitum* diet. Participants consumed the study diet (EU or OF) on days 5-7 and the *ad libitum* diet on days 8-10. Average values for hunger (B), PFC (D), and satiety (F) during the study diet and the *ad libitum* diet period are also presented.

*Significant diet effect, P-value < 0.05

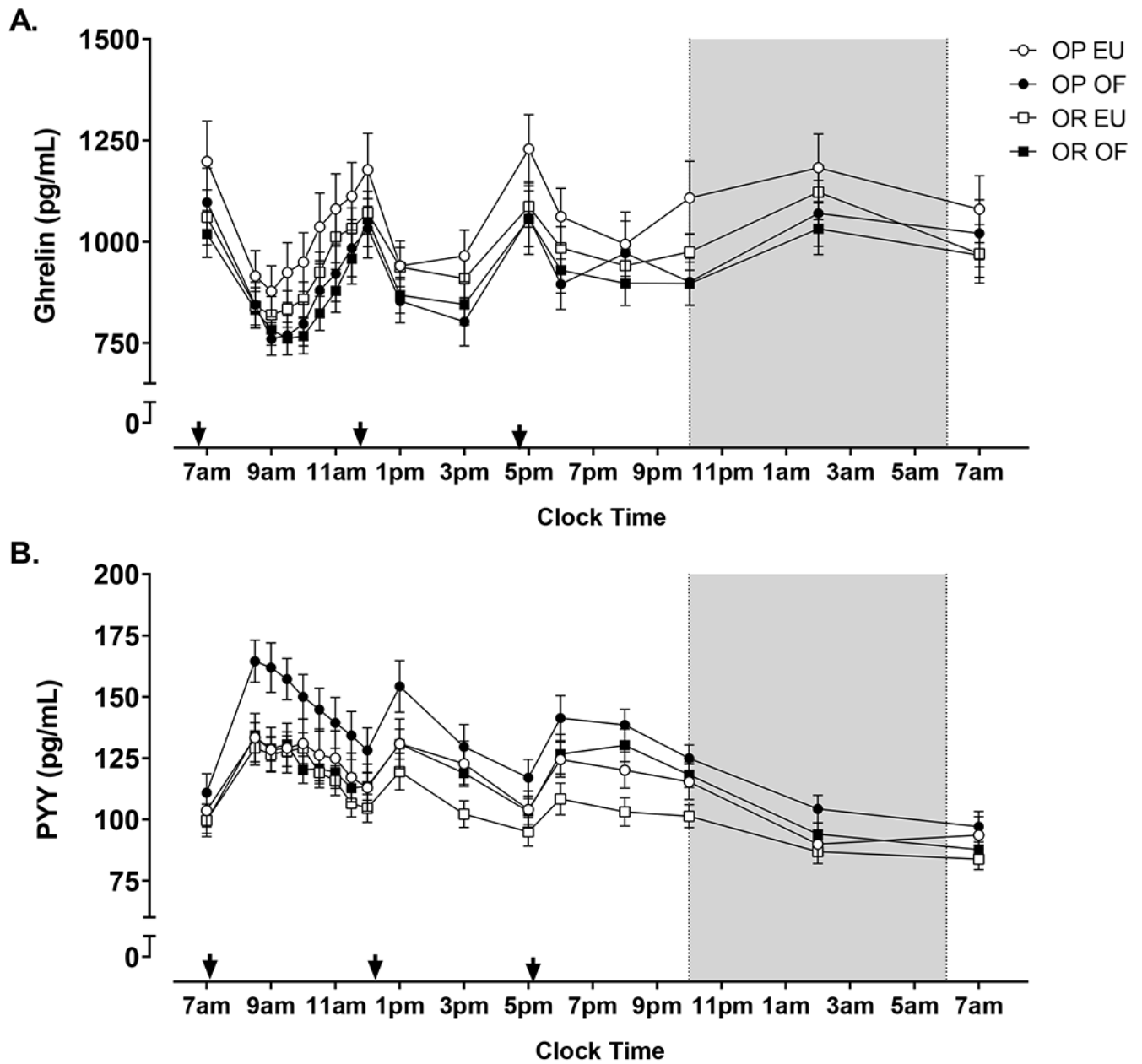


Figure 3.

Twenty-four-hour ghrelin (A) and PYY (B) responses to overfeeding (compared to a eucaloric control diet) in OP and OR adults.

PYY= peptide YY; arrows indicate breakfast, lunch, and dinner, respectively; shaded area indicates sleep opportunity in the room calorimeter

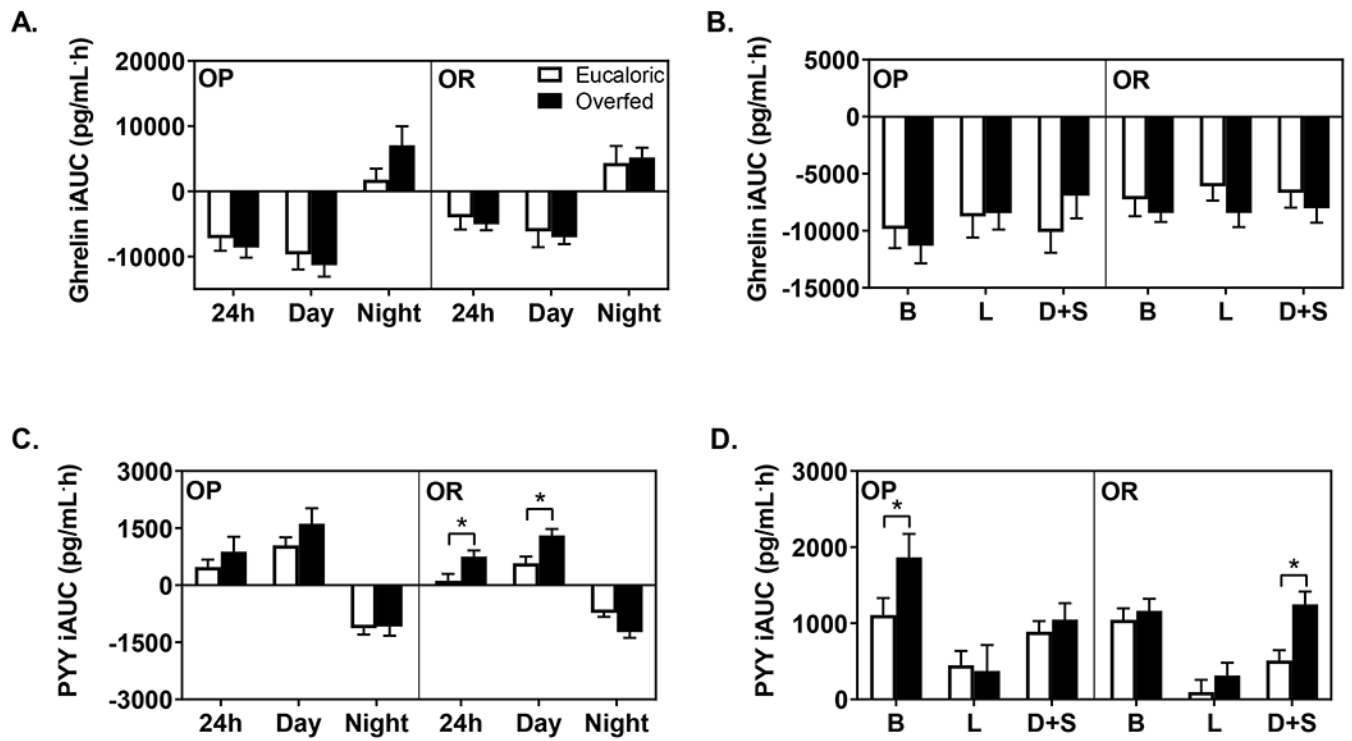


Figure 4.

Summary measures (integrated areas under the curve above baseline) for ghrelin and PYY over 24hr, day, night (A and C), and during feeding periods (B and D) in OP and OR adults studied for 3d under controlled eucaloric (EU) and overfeeding (OF) conditions.

B= breakfast, L= lunch, D+S= dinner plus snack. *Significant diet effect, P-value < 0.05

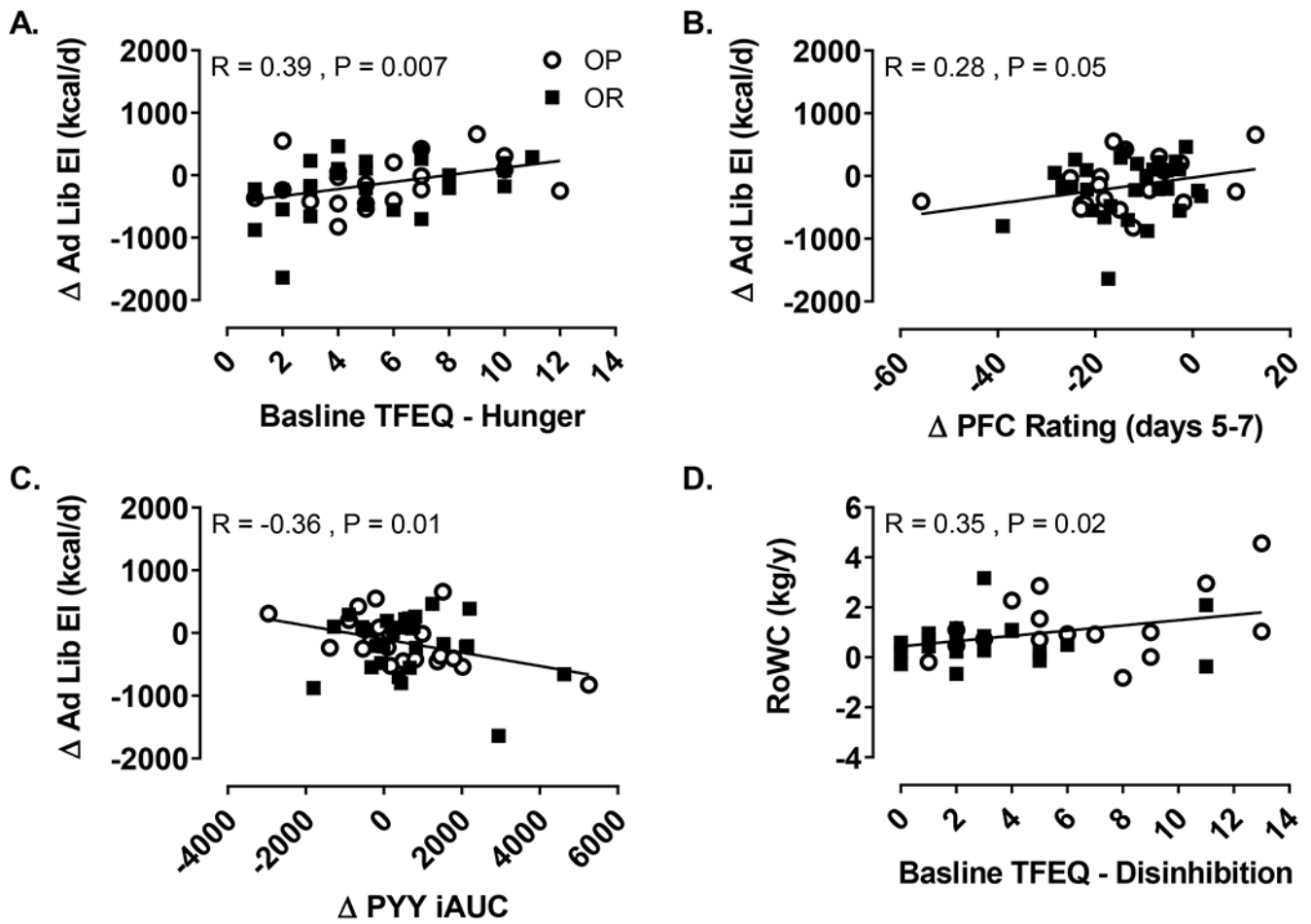


Figure 5.

Correlates of *ad libitum* energy intake and prospective weight gain.

○ = overfed-eucaloric condition, RoWC=rate of weight change. *ad libitum* intake is expressed as the average intake during study days 8 – 10.

Table 1.

Baseline participant characteristics and assessments of dietary restraint, disinhibition and hunger.

	Obesity Prone (OP)	Obesity Resistant (OR)	<i>P</i>
n, (%F)	22 (64)	30 (47)	0.23
Age, yr.	28.5 ± 0.6	28.0 ± 0.5	0.53
Body mass index, kg/m ²	23.9 ± 0.5	20.5 ± 0.4	<0.001
Weight, kg	70.0 ± 2.0	63.5 ± 2.1	0.03
Fat mass, kg	18.4 ± 1.3	11.9 ± 0.5	<0.001
Fat-free mass, kg	51.2 ± 2.1	51.3 ± 2.0	0.98
Baseline TFEQ and PFS			<i>P</i>
TFEQ - Hunger	5.7 ± 0.7	5.1 ± 0.6	0.51
TFEQ - Restraint	7.7 ± 1.1	4.2 ± 0.6	0.005
TFEQ - Disinhibition	6.5 ± 0.8	3.2 ± 0.5	<0.001
PFS	46.3 ± 4.1	35.3 ± 1.5	0.007

%F: percentage of female participants in each group; TFEQ= Three Factor Eating Questionnaire; PFS= Power of Food Scale. Data presented as mean ± standard error.

Table 2.

Bivariate correlations among measures of baseline dietary restraint, subjective and hormonal responses to overfeeding, and *ad libitum* energy intake over a period of three days following overfeeding.

	Ad lib EI (Day 8)	Ad lib EI (Day 9)	Ad lib EI (Day 10)	Ad lib EI (Avg Day 8-10)
TFEQ - Hunger	0.38 (P=0.009) *	0.24 (P=0.11)	0.22 (P=0.14)	0.39 (P=0.007) *
TFEQ - Restraint	0.11 (P=0.45)	0.03 (P=0.87)	0.07 (P=0.63)	0.11 (P=0.46)
TFEQ - Disinhibition	0.15 (P=0.32)	0.20 (P=0.17)	0.06 (P=0.70)	0.20 (P=0.18)
PFS	-0.06 (P=0.69)	0.10 (P=0.49)	-0.11 (P=0.45)	-0.02 (P=0.87)
Pre-meal hunger rating	0.32 (P=0.03) *	0.11 (P=0.44)	-0.05 (P=0.75)	0.16 (P=0.26)
Pre-meal PFC rating	0.40 (P=0.005) *	0.17 (P=0.24)	0.09 (P=0.56)	0.28 (P=0.05) *
Post-meal satiety rating	0.05 (P=0.72)	-0.17 (P=0.25)	-0.19 (P=0.19)	-0.14 (P=0.35)
24 h Ghrelin iAUC	-0.12 (P=0.39)	0.05 (P=0.75)	-0.10 (P=0.48)	-0.08 (P=0.60)
24 h PYY iAUC	-0.26 (P=0.07)	-0.20 (P=0.17)	-0.29 (P=0.05) *	-0.36 (P=0.01) *
Fasting Leptin	-0.13 (P=0.36)	0.04 (P=0.77)	0.13 (P=0.39)	0.04 (P=0.79)

= overfed-eucaloric condition, EI=energy intake, TFEQ= Three Factor Eating Questionnaire, PFS= Power of Food Scale, PYY= peptide YY, iAUC=incremental area under the curve.

Significant differences are indicated with * and bold font.

Table 3.

Bivariate correlations among measures of baseline dietary restraint, subjective and hormonal responses to short-term overfeeding and prospective weight change.

	RoWC (kg/y)	RoFMC (kg/y)
Baseline TFEQ - Hunger	0.19 (P=0.24)	-0.06 (P=0.69)
Baseline TFEQ - Restraint	-0.11 (P=0.49)	-0.29 (P=0.07)
Baseline TFEQ - Disinhibition	0.35 (P=0.02)*	0.05 (P=0.75)
Baseline PFS	0.17 (P=0.30)	-0.03 (P=0.88)
Pre-meal hunger rating	0.08 (P=0.63)	-0.01 (P=0.93)
Pre-meal PFC rating	0.05 (P=0.77)	-0.11 (P=0.47)
Post-meal satiety rating	0.21 (P=0.18)	0.20 (P=0.20)
Ad lib EI (days 8-10)	0.21 (P=0.16)	0.17 (P=0.26)
24 h Ghrelin iAUC	-0.14 (P=0.36)	-0.07 (P=0.66)
24 h PYY iAUC	-0.20 (P=0.19)	-0.02 (P=0.88)
Fasting Leptin	0.21 (P=0.20)	-0.12 (P=0.45)

= overfed-eucaloric condition, RoWC=rate of weight change, RoFMC=rate of fat mass change, EI=energy intake, PYY= peptide YY, iAUC=incremental area under the curve.

Significant differences are indicated with * **and bold font**.