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The Effects of Short-term Overfeeding on Energy Expenditure and Nutrient Oxidation in Obesity Prone and Obesity Resistant Humans

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Abstract

Objective—The roles that energy expenditure (EE) and nutrient oxidation play in a predisposition for weight gain in humans remains unclear.

Subjects—We measured EE and respiratory exchange ratio (RER) in non-obese obesity prone (OP; n=22) and obesity resistant (OR; n=30) men and women following a eucaloric diet and after 3 days of overfeeding (1.4x basal energy).

Results—Twenty four hour EE, adjusted for fat free mass and sex, measured while consuming a eucaloric diet was not different between OP and OR subjects (2367 ± 80 vs. 2285 ± 98 kcals; p=0.53). Following overfeeding, EE increased in both OP and OR (OP: 2506 ± 63.7, p<0.01; OR: 2386 ± 99 kcals, p<0.05). Overfeeding resulted in an increase in 24h RER (OP: 0.857 ± 0.01 to 0.893 ± 0.01, p=0.01; OR: 0.852 ± 0.01 to 0.886 ± 0.01, p=0.005), with no difference between groups in either the eucaloric or overfeeding conditions (p>0.05). Nighttime RER (~10pm-6:30am) did not change with overfeeding in OR (0.823 ± 0.02 vs. 0.837 ± 0.01, p=0.29), but increased significantly in OP subjects (0.798 ± 0.15 to 0.839 ± 0.15, p<0.05), suggesting that fat oxidation during the night was down-regulated to a greater extent in OP subjects following a brief period of overfeeding, as compared to OR subjects who appeared to maintain their usual rate of fat oxidation. Protein oxidation increased significantly in both OP (p<0.001) and OR (p<0.01) with overfeeding, with no differences between OP and OR.

Conclusion—These results support the idea that overfeeding a mixed diet results in increases in EE and RER, but these increases in EE and RER are likely not responsible for obesity resistance. Adaptive responses to overfeeding that occur during the night may play a role in opposing weight gain.

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Keywords

obesity prone; obesity resistant; overfeeding; indirect calorimetry; energy expenditure; fat oxidation; carbohydrate oxidation; protein oxidation

INTRODUCTION

We have been intrigued by the fact that many people maintain a normal weight over their lifetime despite living in the same obesogenic environment that promotes weight gain in most (1). Factors that lead to differences in weight gain between individuals are both behavioral and metabolic (2, 3). Identifying intrinsic metabolic characteristics that predispose some individuals to weight gain may help target prevention efforts to those most likely to gain weight over time. In addition, identifying metabolic factors that protect against weight gain may lay the groundwork for novel therapeutic approaches. While obesity results from an imbalance between energy intake (EI) and energy expenditure (EE), the relative importance that differences in EE play in predisposing to or protecting from excessive weight gain remains controversial (4-6). We wondered if changes in EE produced by a brief period of overfeeding might reveal adaptive responses that relate to a predisposition to weight gain.

Variability in substrate oxidation may be another mechanism underlying a predisposition to weight gain. Longitudinal data show that individuals who rely less on lipid as an energy substrate have a greater tendency to gain body weight and body fat relative to those who oxidize lipid more readily (7, 8). In particular, the ability of an individual to increase or maintain fat oxidation following periods of overeating may be important in that person's ability to resist body fat gain over time. While a number of previous studies have examined the effects of long term overfeeding lasting weeks (9, 10), less is known about the metabolic responses to short term overfeeding in constitutionally thin individuals as compared to those predisposed to obesity. It is possible that individuals predisposed to obesity may not be able to maintain fat oxidation when faced with brief periods of overeating (e.g. 1-3 days), common in today's lifestyle with vacations, holidays, celebrations, etc. The result of this inability to adapt to short term overfeeding would be a state of positive energy and fat balance which, if not compensated for by subsequent reductions in EI or increases in EE, would result in cumulative gains in body weight and fat.

The Energy Adaptations over Time Study (EATS) was designed to examine the role that adaptive responses to short term overfeeding might play in predisposing to or protecting against weight gain. Some of the subjects enrolled came from families where obesity was a problem and who identified themselves as obese prone (OP). Others came from families where obesity was not a problem and identified themselves as constitutively thin or obesity resistant (OR)(11). The aim of this portion of the EATS was to determine if EE and nutrient oxidation were different between OP and OR subjects either during controlled eucaloric feeding or following 3 days of controlled overfeeding. We hypothesized a) 24 hr EE would increase more in response to overfeeding in OR compared to OP subjects, and that b) in response to overfeeding but not eucaloric feeding, OP individuals would demonstrate a

greater reliance on carbohydrate and lesser reliance on fat as a fuel source as compared to OR subjects. The net effect of these responses would be to promote fat storage in OP as compared to OR individuals following short-term overfeeding.

MATERIALS AND METHODS

Subjects

Non-obese men and women ages 25-35 years were empirically classified as OR or OP based on personal and family weight history. OR subjects defined themselves as "constitutionally thin" based on their perception of difficulty gaining weight despite not expending any effort to maintain their weight. These individuals responded to advertisements for "naturally thin people", reported no history of ever being overweight and self-reported a sense that their weight regulation was "different" from other people. They also reported having no 1st degree relatives with a BMI >30 kg/m^2. OP subjects reported having to work to maintain their weight by being conscientious about their food intake and/or activity, but were not actively attempting to lose weight and were weight stable for at least 3 months prior to being studied. These subjects also reported at least one 1st degree relative with BMI >30 kg/m^2.

Preliminary assessments

At baseline, all subjects underwent a physical examination and biochemical testing to exclude medical illness. Subjects were excluded if they took medications known to affect weight or lipid metabolism. They completed questionnaires to exclude eating disorders (12-14) or psychological dysfunction (15, 16). To assess habitual physical activity, subjects wore a pedometer (Digi-Walker, New-Lifestyles, Inc. Lee's Summit, MO) for 1 week. Data on physical activity levels in these subjects using a physical activity monitoring system has been previously reported (11). Body composition was measured by DXA (Hologic Discovery-W, Bedford, MA). Resting EE was measured by hood indirect calorimetry (ParvoMedics Model: TrueOne 2400, Sandy, UT) and 24-hour energy expenditure by whole room calorimetry (17). The energy requirements for free living eucaloric feeding were determined based on REE derived from the average of 1) direct measurement by hood indirect calorimetry and 2) an estimation using the following equation: [(23.9 x FFM in kg) + 372], where FFM was measured by DXA (18). The REE determined from those 2 methods was then multiplied by an activity factor (1.4-1.65), which was based on subjects' average steps taken during the week of baseline pedometer monitoring. To determine energy requirements for the chamber stays during the experimental interventions, TEE was directly measured during a "baseline" 23-hr stay in the room calorimeter (independent of and before the study periods reported). This value for TEE in the chamber was compared to the "free living" TEE estimated by the method outlined above. TEE in the room calorimeter was found to be about 8% less than the TEE calculated from free living TEE values. Therefore, subjects were fed 8% fewer calories on the day that they were in the calorimeter.

Study Design

Subjects were studied on the Clinical Translational Research Center (CTRC) at the University of Colorado Anschutz Medical Campus on two occasions separated by at least 1 month. For the first 4 days of each study period, subjects consumed a eucaloric "run-in diet"

(20% protein, 34% fat, 46% carbohydrate) to ensure energy and nutrient balance. For the next 3 days, participants consumed, in random order, either a controlled eucaloric (EU) diet or a controlled hypercaloric diet (OF) containing 1.4 X estimated energy needs. The macronutrient content of each study diet was the same as that of the lead in diet and was consumed under free-living conditions. During each study period, we confirmed that subjects consumed only food and beverages provided by the CTRC metabolic kitchen.

Calorimetry Days

On the third day of each controlled diet period, subjects spent 23 hours in the whole-room calorimeter. The CTRC's whole-room calorimeter was used to measure substrate oxidation and 24-h EE. Data on EE and substrate oxidation collected over the 23-h time window (0800-0700) were extrapolated to 24 h for purposes of data analysis. During each stay in the calorimeter, subjects consumed a diet estimated to achieve energy balance or to produce a 40% overfed state. O_2 consumption and CO_2 production were determined from the air flow rates and differences in gas concentrations between air entering and air exiting the calorimeter, as previously described (19). Energy expenditure and substrate oxidation were calculated from O_2 consumption and RER based on equations described by Jequier et al. (20). Protein oxidation was estimated from 24-h urinary nitrogen excretion, and carbohydrate and fat oxidation were estimated using NP-RER values (21). Values for all indices were averaged over 1-minute intervals and recorded to a data file.

On the study day, breakfast (25% of daily energy) was given to subjects at 0730, which was considered time zero, and consumed within 20 min. Participants then entered the calorimeter at 0800 h. Lunch and dinner were given at 1200 and 1700 (both meals contained 30% of daily energy), with a snack (15% of daily energy) given at 2000. All meals were consumed within 30 min of being served. The subjects went to bed at 2200 and subjects exited the chamber at 0700 h the following morning. In order to approximate normal activity levels outside the calorimeter, each subject performed two bouts of stepping. The objective of this exercise was to increase the EE of the subject in the calorimeter to roughly the same level that he/she would normally experience under free-living conditions. Specifically, starting at 1430 and then again at 1630 h, subjects performed 10-min of walking, followed by 10 min of sitting quietly, then 10 min of stepping and finally 10 min of sitting. Rates of walking and stepping were specified and constant for all subjects.

Statistical Analyses

Data were analyzed using SPSS version 19.0 (Cary, NC). A repeated measures analysis of variance (ANOVA) was used to examine differences in macronutrient oxidation and EE during the OF and EU study periods among OP and OR subjects, with p-values identified for interactions and main effects of group (OP vs. OR) and diet phase (EU vs. OF). For significant interactions, Bonferroni post-hoc tests were performed to determine within group differences between conditions. If the interaction terms were non-significant, then the main effects of group and diet phase were evaluated. Energy expenditure was adjusted for sex and FFM, while RER was adjusted for age, FFM and sex, based on these variables being independently correlated to the outcome variables. Adjusted means and standard errors for energy expenditure (EE) and RER were reported for the total 24h period, during the night,

and during the daytime in both EU and OF study periods. Values for EE during the daytime and nighttime periods were extrapolated to 24h. In making sex-based comparisons, FFM was used as a covariate in the ANOVA. For correlation analysis, we used bivariate Pearson's correlation analysis, using a two-tailed test of significance.

The daytime period began when subjects entered the calorimeter, and it ended when the nighttime period began, which was at approximately 10:00 pm, but was individually determined from the calorimetry data by examining the drop and stabilization of EE (presumably when subjects were asleep) and rise and stabilization of EE (presumably when subjects awoke), which occurred at roughly 6:30 am. A half hour time period in the middle of the night (~2:00am-2:30am, based on elevated EE) was excluded, as subjects were awakened for a blood sample; we therefore also analyzed the time from 3:30am-5:00am (referred to below as "late night") since sleep was uninterrupted during this time. The statistical significance was set at $p<0.05$, with two-tailed tests used for changes in EE and RER.

RESULTS

Subject characteristics are displayed in Table 1. Fifty-two subjects (22 OP, 30 OR) completed both EU and OF study periods, with no drop outs once subjects were initially enrolled in the study. Subjects in the two groups were non-obese (BMI <27kg/m^2 for all subjects) and matched with regards to age, fat-free mass, and RMR (Table 1). Obesity prone subjects had significantly higher FM, trunk fat, percent body fat and BMI compared to OR subjects ($p<0.05$) although the mean BMI in the OP group (23.5 ± 2.6) was well below the cutoff for overweight. Body weight did not change between the eucaloric (66.63kg ± 1.6) and overfed (66.57kg ± 1.6) study periods for all subjects ($p>0.05$), with no differences between OP and OR for the change in body weight between study periods ($p>0.05$).

Energy Expenditure

Table 2 displays EE for all subjects during the two diet phases. Energy expenditure was not significantly different between OP and OR subjects during the eucaloric or overfed study periods ($p>0.05$), and there was no significant group x diet interaction ($p>0.05$). Short term overfeeding led to a significant increase in EE for both OP ($p<0.01$) and OR ($p=0.04$) subjects for both 24h EE and EE during daytime hours (OP: $p<0.01$; OR: $p=0.02$). However, nighttime and late night EE did not significantly change following overfeeding in either group ($p>0.05$). The frequency distribution of the change in 24h EE for OP and OR is shown in Figure 1. There was no difference in the distribution of change in 24h EE between OP and OR (+139 ± 48 vs. +101 ± 44 kcals, respectively, $p=0.6$). Since overfeeding for several weeks can lead to an increase in lean body mass (10), we examined the relationships between 24hEE and protein oxidation. While a significant correlation was found between 24h EE and 24h protein oxidation in both the EU (OP: $r=0.6$, $p<0.01$; OR: $r=0.4$, $p<0.05$) and OF (OP: $r=0.7$, $p=0.001$; OR: $r=0.6$, $p<0.001$) periods in both groups, we found no correlation between the change in 24h EE and the change in protein oxidation in either OP or OR subjects (r-value was less than 0.1, $p>0.6$ for both groups) or in the group taken as a whole.

Differences between energy expenditure in men and women were also examined after controlling for FFM. There was not a significant sex x diet phase interaction (p=0.28) for 24h EE; nor were there significant differences between sex during the eucaloric (M: 2244 ±102; W:2382 ±87 kcals, p>0.05) study period; however during the overfed period, females had greater 24h EE compared to males (M: 2289 ± 80; W: 2575± 68 kcals, p<0.01) when all females were compared to all males. We found that when men were compared to women within each obesity risk group, there were no sex-based differences in the OP group, and the OR group only differed in night time EE during the OF condition, with women having significantly greater night time EE than men (1594 ± 67 vs. 1321 ± 60, p<0.05).

Pedometers were worn in the calorimeter to measure physical activity. There was a significant group x diet interaction (p<0.05) for number of steps taken while in the calorimeter. OP subjects significantly decreased their steps in the room calorimeter in the overfed as compared to the eucaloric study phases (EU: 5385±400; OF: 4409±460 steps, p=0.02), while OR subjects did not significantly change their total steps taken from eucaloric to overfed study periods (5081± 331to 5176±282 steps, respectively, p=0.78). However, steps taken by OP subjects did not significantly differ from OR in the eucaloric (p=0.56) or overfed study periods (p=0.07). In addition, men and women did not differ in the number of steps taken while in the calorimeter or in the change in daily steps taken between the EU and OF conditions (p>0.05).

These results indicate that overfeeding does not result in greater increases in EE in OR as compared to OP subjects, suggesting that increases in EE following overfeeding do not contribute to obesity resistance.

Macronutrient oxidation

Short term overfeeding led to significant changes in RER (Table 3). Overfeeding resulted in higher non-protein RER for both OP and OR subjects during the total 24h period compared to the eucaloric study period, with no significant group x diet phase interaction (p=0.94), and no differences between groups for either diet phase (p>0.05). For RER during the daytime, there was not a significant group x diet interaction (p=0.96) or main effect of group (p=0.66), but there was a significant main effect of diet phase, with RER increasing with overfeeding (p=0.01). This change in RER with overfeeding was not statistically significant in OP, (p=0.14), but did reach statistical significance in OR subjects (p=0.04), with no differences between OP and OR during either study period. RER during the nighttime increased significantly with overfeeding only in OP (p=0.04) but not in OR (p=0.31), although the interaction was not significant (p=0.26). For late night (3:30-5am) RER, there was not a significant group x diet interaction (p=0.49) or main effect of group (p=0.43), but there was a significant main effect of diet phase, with RER increasing with overfeeding (p=0.01). The late night RER increased significantly with overfeeding only in OP (p=0.03) and not in OR (p=0.20).

Substrate oxidation was calculated from oxygen consumption and RER using previously described equations (20). Figure 2 shows that overfeeding led to a significant increase in carbohydrate oxidation over a 24h period in OP (1017.9±79.7 vs. 1394.1±100.0 kcals, p<0.01) and OR (968.9±91.4 vs. 1239.9±74.0 kcals, p<0.01) subjects, with no difference

between OP and OR for either study phase (p>0.05). Protein oxidation (as estimated by urinary urea nitrogen excretion) also significantly increased with overfeeding in both groups (OP: 423.7±22.7 vs. 527.4±26.3 kcals, p<0.001; OR: 467.3±20.8 vs. 544.5±22.7 kcals, p<0.01), with no difference between OP and OR in either study phase (p>0.05) (Figure 2). Fat oxidation decreased with overfeeding in OP (911.3±88.2 vs. 650.2±81.3 kcals, p=0.01) and OR (898.3±100.9 vs. 674.8±71.7 kcals, p=0.02), also with no difference between OP and OR in either study phase (p>0.05) (Figure 2).

Differences between RER in men and women were examined after controlling for FFM. We found that when all men were compared to all women, there was no significant sex x diet phase interaction or main effect of sex (p>0.05), and there were no significant differences in 24h RER or for any time segment throughout the day (p>0.05). In addition, there were no significant differences in men or women in the change in RER for any time point (p>0.05).

These results suggest that overfeeding a mixed diet leads to an overall increase in RER in both OP and OR groups, with small differences seen in the changes during the day vs nighttime. However, there were no significant differences between OP and OR at any time over the entire 24h period. These differences between study phases indicate that more carbohydrate, more protein, and less fat were oxidized throughout the day when subjects were overfed compared to what was oxidized when subjects were in energy balance. OR subjects did not have a change in their RER during the nighttime when the eucaloric study period was compared to the overfed period; whereas, OP subjects did not significantly alter their daytime RER with overfeeding (changes in protein oxidation were only measured for the 24h period, not day vs night). Taken together, we found that there are only modest differences in macronutrient oxidation with overfeeding in OP and OR subjects, and these slight differences in response to overfeeding may be attributable to differences in substrate oxidation during the day vs. night time.

DISCUSSION

The main findings of this study are that non-obese individuals who are prone or resistant to obesity consuming a eucaloric diet do not significantly differ in their EE or macronutrient oxidation. Following a period of short-term overfeeding, 24 h EE increased in all subjects which is consistent with what previous overfeeding studies have shown (22, 23). In contrast to what was originally hypothesized, following overfeeding, 24 h EE did not increase to a greater extent in OR as compared to OP subjects. Short term overfeeding also resulted in an increase in RER and urinary nitrogen excretion, suggesting an increase in carbohydrate and protein oxidation and a decrease in fat oxidation in both OP and OR subjects as compared to levels observed during the eucaloric diet phase. These findings are consistent with what has previously been shown with overfeeding a mixed diet (22, 24). It has been shown that when obese individuals are overfed, they have a greater suppression of fat oxidation than lean overfed subjects (25). However, this is the first set of data to show that non-obese individuals who are prone or resistant to obesity have a similar change in fuel utilization over 24h following short-term overfeeding. Taken together these data do not support the idea that OR individuals have unique metabolic adaptive responses to overfeeding that help them prevent weight gain. However, when daytime and nighttime periods were examined

separately, a somewhat different picture was seen. While 24h fat oxidation fell in all subjects following overfeeding, there was no decrease in nighttime fat oxidation in OR subjects with overfeeding. These results suggest that OP individuals may have a shift in metabolism at night that results in lower fat oxidation following a period of overfeeding compared to individuals resistant to obesity. Of note, protein oxidation during the night was not specifically measured in this study, and to our knowledge, no studies have examined how nocturnal protein metabolism responds to overfeeding in obese or obese prone subjects. Although the differences in the responses in nocturnal metabolism to overfeeding in OP and OR individuals were small in comparison to the energy and fat load delivered during the period of overfeeding, these changes along with other maladaptive responses, including changes in protein oxidation, may contribute to future weight gain in OP individuals following overfeeding.

The role that differences in EE play in weight gain is controversial (26). Studies in Pima Indians initially suggested that low EE predisposes to weight gain (27, 28). This relationship was also found in individuals with mutations in the MC4R (29) and were also initially found in children born to obese parents (30). However, more recently this relationship has not been found in a number of populations prone to weight gain(31-33). Counter intuitively a number of well-done studies have found that higher levels of EE are associated with weight gain (5, 34). We wondered whether short term overfeeding would bring out differences between OP and OR individuals that might not have been seen when studies were conducted in a eucaloric state. Previous studies have shown that EE increases to a variable degree following overfeeding and that some of the observed differences might be related to changes in spontaneous physical activity (9). In a prior analysis of direct measures of physical activity from this same cohort of subjects, we found minimal evidence for this view (11). Overall we did not find evidence in support of the view that changes in EE in response to overfeeding protect against weight gain, a view held by many constitutively thin individuals.

The idea that reduced levels of fat oxidation are causally related to weight gain has also gained traction recently (35, 36). Studies in Pima Indians support this view (37) as do some studies carried out in reduced obese individuals (38). However, studies in groups at risk for weight gain do not support this hypothesis (39). We previously conducted studies in animal models of obesity which led us to the idea that reductions in the oxidation of dietary fat (40) especially following a period of passive overfeeding (41) predispose to weight gain. Here again we reasoned that a period of overfeeding might bring out differences in fat oxidation between OP and OR individuals. The traditional view is that if fat is not oxidized it would be stored promoting an increase in fat mass. However, this assumes that energy intake or fat intake does not change. For energy balance to occur there must be communication between the periphery and the central nervous system about the state of energy/nutrient balance (42). For a reduction in fat oxidation to be causally related to weight gain, it would have to be a sign of a metabolic alteration that results in a reduction in the accuracy of information on the peripheral state of energy balance to the brain.

The present study suggests that the metabolic differences between OP and OR individuals either in the eucaloric state or following short term overfeeding are modest. These results may highlight the role that adaptive responses to overfeeding that occur during day vs. night,

including relative differences in fat oxidation, may play in opposing weight gain. A number of studies have highlighted the adverse effects of reduced sleep time and shift work on weight and metabolic health (43). However the exact role that sleep plays in maintaining normal metabolism is not clear. Virtually all tissues of the body express clock genes that regulate circadian rhythms (44). Presumably these genes regulate metabolic processes in response to the typical pattern of food consumption during daytime and fasting during the night. While the body needs to respond quickly to acute metabolic challenges like bouts of exercise and meal ingestion during the day, the nighttime is a period of relative stability during which the body may integrate the net changes in energy balance that occurred during the previous day and "reset" the internal state in preparation for the next day. It may be that important insights into the adaptive responses to energy imbalance, will come from studies of metabolic processes and hormones at night.

There are a number of important limitations of the current study. While a strength of the study is that we measured metabolic responses to overfeeding in people who were not yet obese but had a propensity to gain weight or remain thin, the methods used to categorizing subjects as OP or OR may not be entirely accurate. Much of the categorization relied on the subjects' perception of their tendency to gain weight or not. We are following these individuals' weight prospectively over time, and we have already seen individuals who were initially categorized as OP who made a conscious decision to lead a healthy lifestyle to minimize weight gain so that they would not develop the health problems that they had seen family members endure. Conversely, several OR subjects have undergone life events, such as changes in employment and family issues, that resulted in substantial weight gain. These events demonstrate that longitudinally determined weight gain may not be a better reflection of a biological predisposition than subjects' own sense of their predisposition to weight gain. A second limitation is the fact that urine was collected continuously over 24 h for urea nitrogen and not separated as daytime and nighttime samples; therefore, we cannot comment on diurnal variations in protein oxidation which may in part explain differences seen in nutrient oxidation between day and night. A final limitation is the restrictions on physical activity imposed by the room calorimeter. Differences in physical activity could significantly impact 24 h EE in free living individuals. However, as noted above, we did not find evidence of this in direct measures of physical activity conducted in these subjects in free-living conditions.

In summary, the results of this study support the idea that overfeeding results in increases in EE which partially offset the positive energy balance associated with overfeeding. The results confirm the important impact that positive energy balance plays in nutrient preference promoting carbohydrate and protein oxidation and concomitantly reducing fat oxidation. The results do not support the widely held belief that constitutively thin people have higher metabolic rates and respond to overfeeding with protective increases in EE and fat oxidation. The main differences between OP and OR subjects identified following overfeeding occurred in diurnal and nocturnal metabolism. It may be that future studies should focus on the impact of states of energy imbalance on nocturnal or diurnal metabolism and related hormones and the role that these changes play in the regulation of body weight.

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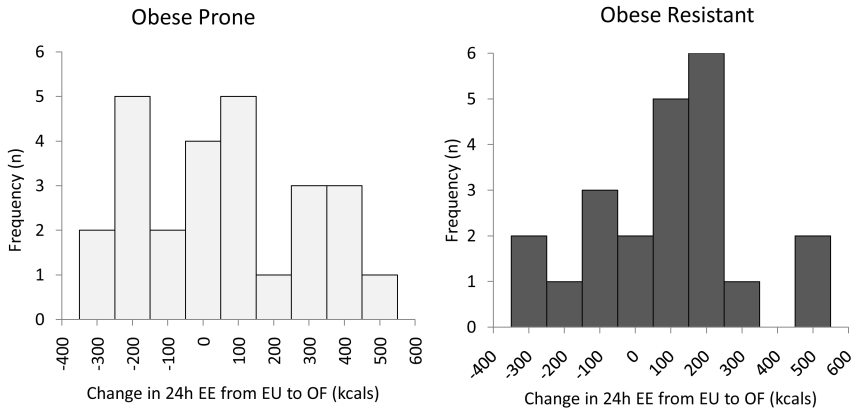

Figure 1.

Frequency Distribution for change in 24h EE (24h EE in OF-EU study phases) in Obese Prone (OP) and Obese Resistant (OR) subjects.

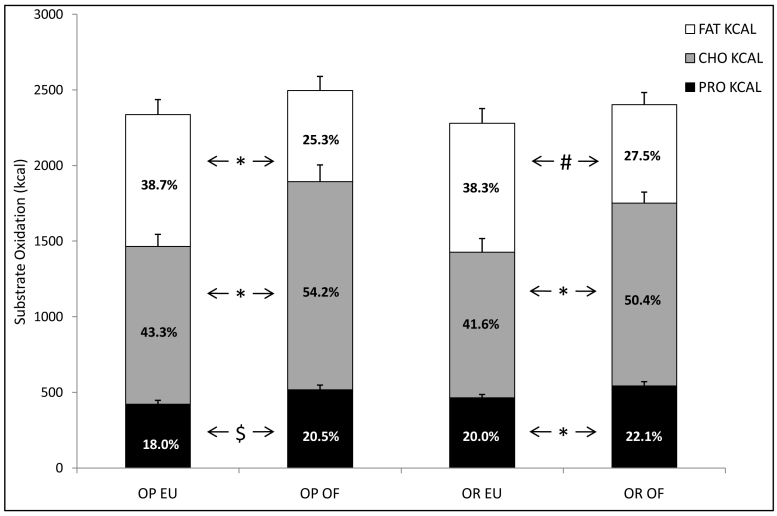

Figure 2.

Macronutrient Oxidation over 24h in Obese Prone (OP) and Obese Resistant (OR) subjects in the Eucaloric (EU) and Overfed (OF) study periods. $ $p<0.001$, *$p<0.01$, # $p<0.05$ for EU vs. OF within obesity group for each macronutrient.

Table 1

Subject Characteristics. Values are means ± SD.

	Obese Prone (OP)		Obese Resistant (OR)	
	Males	**Females**	**Males**	**Females**
n	**8**	**14**	**16**	**14**
Age	28.6 ± 2.2	28.4 ± 2.2	28.1 ± 2.9	27.9 ± 2.2
BMI (kg/m^2)	24.8 ± 1.6	22.7 ± 1.8	21.7± 2.2$^{\#}$	19.6 ± 1.7°
Fat Free Mass (kg)	62.8 ± 2.6	44.6 ± 4.4	60.0 ± 7.2	41.4 ± 4.8
Fat Mass (kg)	14.8 ± 4.4	19.1 ± 4.8	11.0 ± 3.2*	12.9± 2.4°
Trunk fat (kg)	7.4 ± 2.7	8.3 ± 2.7	5.1 ± 1.6*	4.9 ± 1.2°
Body Fat (%)	18.8 ± 4.9	29.6 ± 4.7	15.3± 3.2*	23.7± 4.0°
Trunk Fat (% of body fat)	49.0 ± 5.4	42.9 ± 3.9	46.5 ± 2.2	38.5 ± 4.6
RMR (kcal/day)	1734 ± 126	1438± 180	1716 ± 246	1354 ± 186
Calorie intake EU	2684 ± 117	2143 ± 261	2689± 323	2000 ± 186
Calorie intake OF	3483 ± 396	3138 ± 391	3239 ± 368	3165± 369

* $p<0.05$,

$^{\#}$ $p<0.01$

$^{\circ}$ $p<0.001$ significant difference between obesity group, within sex

Table 2

Energy Expenditure (EE) in the whole-room calorimeter for the total 24h period, during daytime period only, during the nighttime, and late night (3:30am-5am) for Obese Prone (OP) and Obese Resistant (OR) subjects in the Eucaloric (EU) and Overfed (OF) study periods. Values are means and standard errors extrapolated to 24 hours. Late night values were not extrapolated to 24h.

	Total EE (kcal)	Daytime EE (kcal)	Night time EE (kcal)	Late night EE (kcal)
Obese Prone-EU	2372 ±66	2904 ± 78	1361 ± 60	81.4 ± 3.8
Obese Prone-OF	2482 ± 51#	3069 ± 75#	1448 ± 43	82.9 ± 2.6
Percent change	+4.6% ± 2.0	+5.7% ± 2.0	+6.4% ± 5.3	+1.8% ± 5.6
Obese Resistant-EU	2283 ± 58	2781 ± 68	1376 ± 52	79.7 ± 3.3
Obese Resistant-OF	2393 ± 44*	2909 ± 65*	1456 ± 38	85.1 ± 2.3
Percent change	+4.8% ± 2.5	+4.6% ± 2.2	+5.8% ± 4.6	+6.7% ± 4.0

* $p<0.05$

# $p<0.01$ for EU vs. OF within obesity group

Table 3

Respiratory Exchange Ratio (RER) in the whole-room calorimeter for the total 24h period, during daytime period only, during the nighttime, and late night (3:30am- 5am) for Obese Prone (OP) and Obese Resistant (OR) subjects in the Eucaloric (EU) and Overfed (OF) study periods. Values are means and standard errors.

	24H RER	Daytime RER	Night time RER	Late night RER
Obese Prone-EU	0.857 ± 0.01	0.870 ± 0.01	0.798 ± 0.15	0.795 ± 0.01
Obese Prone-OF	0.893 ± 0.01*	0.896 ± 0.02	0.839± 0.15#	0.841 ± 0.02#
Obese Resistant-EU	0.852 ± 0.01	0.865 ± 0.01	0.823 ± 0.13	0.812 ± 0.01
Obese Resistant-OF	0.886 ± 0.01*	0.898 ± 0.01#	0.837 ± 0.14	0.833 ± 0.01

*$p<0.05$

#$p<0.01$ for EU vs. OF within obesity group