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Macronutrient intake associated with weight gain in adolescent girls with anorexia nervosa

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Abstract

Adolescents and women with anorexia nervosa (AN) are known to severely restrict total calorie and fat intake. However, data are limited regarding specific macronutrient intake associated with weight gain in AN.

Objective—To prospectively investigate dietary macronutrient composition associated with weight gain in adolescent girls with AN.

Method—A prospective naturalistic study of 90 girls 12–18 years old; 45 with AN and 45 healthy normal-weight-controls over a 6–12-month period. Participants completed four-day food diaries and underwent body composition assessment using dual energy x-ray absorptiometry. Weight gain was defined as a ≥10% increase in BMI from baseline.

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Authors' Contributions to the manuscript:

1. Charumathi Baskaran: interpreted data, wrote the manuscript with Ms. Carson, and critically reviewed the manuscript
2. Traci Carson: analyzed data and performed statistical analysis, wrote the manuscript, and has primary responsibility for final content
3. Karen J. Campoverde Reyes: analyzed data, performed statistical analysis, and critically reviewed the manuscript.
4. Kendra Becker: Critically reviewed the manuscript
5. Shreya Tulsiani: conducted the research, provided essential materials, and critically reviewed the manuscript
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8. Madhusmita Misra: designed the research, interpreted the data, and critically reviewed the manuscript.
9. Anne Klibanski: designed the research and critically reviewed the manuscript

Results—Baseline clinical characteristics did not differ between girls with AN who did not gain weight (AN-0) versus those who did (AN-1) over the following 6–12 month period except for percentage of calories from proteins (p=0.02). At 6–12 month follow up, AN-1 consumed a lower percentage of total calories from protein (p=0.001), and a higher percentage of total calories from fat (p=0.02) compared to AN-0. AN-1 had a significant increase in the percentage of total calories obtained from mono-unsaturated-fatty acids (MUFA) (p=0.02) and poly-unsaturated-fatty acids (PUFA) (p=0.007) compared to AN-0, between baseline and follow up. Within the AN group, BMI at follow-up was associated positively with percentage of total calories obtained from fat, MUFA, and PUFA ($p<0.05$) at 6/12 months, and inversely with the percentage of total calories obtained from carbohydrates and proteins (p=0.03).

Discussion—Consuming a greater proportion of total calories from fat is associated with weight gain in adolescent girls with AN.

Anorexia nervosa (AN), a psychiatric disorder that commonly occurs during adolescence (Brambilla et al., 2003), is characterized by a distorted body image, a pathological fear of weight gain, and excessive dieting that leads to severe weight loss (DSM-5). Severe caloric restriction suppresses the hypothalamic-pituitary-gonadal (HPG) axis leading to amenorrhea (Brambilla, et al., 2003), and disrupts other endocrine axes as well leading to bone loss (Misra et al., 2004) and increased fracture risk (Faje et al., 2014; Vestergaard et al., 2002). Neuro-psychiatric co-morbidities such as depression and anxiety are also common (Lawson et al., 2009; Lawson et al., 2012; Miller et al., 2007).

Although weight gain is a necessary pre-requisite for recovery of normal endocrine function (van Elburg et al., 2007), macronutritional components that predict weight gain in AN are not well understood (Herpertz-Dahlmann, Wewetzer, Schulz, & Remschmidt, 1996). Intense fear of gaining weight is a critical component of AN, and recovery requires attention to both physical and psychological domains (Misra et al., 2006; Windauer, Lennerts, Talbot, Touyz, & Beumont, 1993). Adolescents and women with AN have an aversion to dietary fat and severely restrict fat intake and consume high amounts of fiber (Drewnowski, Pierce, & Halmi, 1988; Fernstrom, Weltzin, Neuberger, Srinivasagam, & Kaye, 1994; Hadigan et al., 2000; Misra, et al., 2006), which is known to be inversely associated with estrogen status, nutrient absorption, and metabolizable energy (Baer, Rumpler, Miles, & Fahey, 1997; Gaskins, Mumford, Wactawski-Wende, & Schisterman, 2012; Gaskins et al., 2009). However, little is known about macronutrient intake, including fat and fiber intake, that may be associated with weight gain in AN.

Our study addresses this gap by prospectively investigating macronutrient composition associated with weight gain over a 6–12 month follow-up period in a cohort of adolescent girls with AN. We hypothesized that AN girls who achieve weight gain (≥10% increase in baseline BMI) (Soyka et al., 2002) have an increased intake of dietary fat.

PARTICIPANTS AND METHODS

Participant Selection

Data from previous studies from our group conducted from 1998 to 2010 were pooled to determine the macronutrient composition of diet associated with weight gain in community

dwelling girls with AN 12–18 years old. One hundred and seventy-six adolescent girls with AN and 112 controls were enrolled in these studies. Fifty two girls with AN who were on estrogen treatment at follow-up were excluded from the analysis. Controls with a BMI ≥25 were also excluded from analysis. After excluding these participants, both baseline and follow up nutrition data were available for 45 AN girls and 45 controls; therefore, 90 participants were included in the final analysis. Only baseline nutrient intake has been previously reported for some of the participants included in the current study (Misra, et al., 2006). We now report the differences in macronutrient data at follow-up in AN girls who gained weight and those who did not.

Participants with AN met DSM-IV criteria for the disorder (as enrollment occurred prior to publication of DSM 5), including absence of menses for at least three consecutive months preceding study enrollment (A. P. Association, 2000). AN participants were recruited from Massachusetts General Hospital (MGH), community providers and treatment centers. The diagnosis of AN was confirmed by communication with the subject's primary care physician/eating disorder specialist/therapist and by the study psychiatrist or clinical psychologist. Healthy adolescents in the same age range (controls) were recruited through mailings to primary care pediatric practices in and around Boston and via newspaper advertisements. Controls were of normal body weight (BMI between the 10^{th}–90^{th} percentiles for age and <25 kg/m^2), and reported regular menstrual periods and no history of amenorrhea (when postmenarchal) or disordered eating. Because the studies from which participants were drawn had endpoints related to bone density, all participants were screened for diseases known to affect bone metabolism and medications known to affect bone metabolism and the use of oral contraceptives within three months of study enrollment.

The study protocol was approved by the Partners Institutional Review Board and complied with the Health Insurance Portability and Accountability Act guidelines and written informed assent and consent were obtained from all participants and/or their legal guardian.

Experimental Protocol

Participants were evaluated at our Clinical Research Center (CRC) at baseline, 6 and/or 12 months. The baseline visit included a history and physical examination. At baseline, we analyzed macronutrient intake in all girls with AN and controls, and prospectively compared nutrient intake in girls with AN who did or did not gain weight, as defined by ≥10% increase in baseline BMI (Soyka, et al., 2002). For follow-up, we compared food records for girls with AN who gained weight versus those who did not over 6–12 months. For participants who did not have 12-month follow-up data, we included 6-month follow-up data if these were available. Twelve-month data were available for 34 AN participants and 38 controls and 6-month data for an additional 11 AN participants and 7 controls. For participants without 12-month data, 6-month data were carried forward for analysis.

Nutrient Intake

Participants completed a 4-day food diary (three weekdays and one weekend day) to assess dietary intake following detailed instructions provided by registered CRC dieticians. The 4-day food diary correlates better with estimates of individual food consumption than 24-hour

recalls and a detailed quantitative two-month food history (Morgan, 1978), and was therefore chosen over other dietary assessment methods. Research dietitians reviewed the completed food records with each participant at time of visit to clarify food portions and preparation. Food models were used to guide determination of food quantity. Food items were data entered in a comprehensive nutrient database, Minnesota Nutrition Data System software. Upon data entry, analysis was completed and reviewed by registered dietitians for completeness and accuracy in data entry.

Similar numbers of participants who did or did not gain weight were available from the three protocols that formed the basis of this study (eight and nine from protocol 1, six and five from protocol 2, and nine and eight participants from protocol 3 respectively). Given that the number of participants who did vs. those who did not gain weight was well balanced across the three protocols, any effect of the timing of the specific study should be equally distributed across the groups.

Anthropometric Data and Body Composition

Height was measured with a single stadiometer, and weight was measured using an electronic scale while participants were wearing a hospital gown. Body mass index (BMI) was calculated as the ratio of weight (kg) to height (m) squared. We calculated BMI z-scores using National Center for Health Statistics Database (NCHS 2000) (Golden et al., 2015). For all participants, percent body fat, and lean and fat mass were assessed using dual-energy x-ray absorptiometry (DXA).

Statistical Analysis

We used JMP (version 11; SAS Institute, Inc., Cary, NC) for all data analyses. Data are described as means ± SEMs for variables that were normally distributed, and as median and inter quartile ranges for variables that were non-parametric in distribution. For continuous variables, the Student's *t* test and ANOVA were used to determine differences between groups when data were normally distributed, and the Wilcoxon Rank Sum test of Kruskal Wallis test were used when data were not normally distributed (for two and three group comparisons respectively). Tukey Kramer and Steel-Dwass tests were used to control for multiple comparisons for parametric and nonparametric data, respectively. We also performed analysis of covariance (ANCOVA) to determine differences between AN-0 and AN-1 groups for 6/12 macronutrient intake after controlling for baseline energy intake or for the respective baseline macronutrient intake. Pearson correlations were used to identify associations of specific macronutrient intake with weight gain in the AN group. Significance was defined as $p < 0.05$ for all statistical analyses.

RESULTS

Clinical Characteristics and Body Composition in AN and Control Groups

Participant characteristics at baseline are shown in Table 1. Girls with AN were about a year older than controls, and as expected, had significantly lower BMI, BMI z-scores, fat mass, and percent body fat compared with controls. Lean mass trended lower in girls with AN.

At baseline, clinical characteristics and body composition measurements did not differ significantly between AN girls who did not achieve weight gain (AN-0) and those whose BMI increased by at least 10% during follow-up (AN-1) (Table 1). However, as expected per study design, at follow up, the AN-1 group had significantly higher BMI, BMI z-scores, percent body fat, lean mass and fat mass, compared to AN-0 (Table2). Of note, body composition changes with increasing age during puberty, with increases in percent body fat in girls through the pubertal years (Loomba-Albrecht & Styne, 2009). Further, percent body fat is a major predictor of future weight gain and recovery in AN (Mayer et al., 2007). Thus, we also controlled for age in these analyses, and body composition differences between AN-0 and AN-1 groups persisted at follow up. Further, we examined body composition changes in AN girls who recovered menses and achieved weight gain vs. those who did not recover menses and/or achieve weight gain. At follow-up, AN girls who recovered menses and gained weight (n=9) had higher BMI (21.6±0.6 vs. 18.0±0.4 kg/m^2, $p<0.001$), percent body fat (26.8±2.3 vs. 19.0±1.0%, p=0.002), and total fat mass (15.5±1.7 vs. 9.3± 0.7 kg, p=0.0002) compared to those who did not recover menses and/or gain weight (n=28). Data regarding menstrual recovery were not available for the remaining individuals (n=8) and these participants were thus not included in this analysis.

Macronutrient Intake at Baseline in AN and Control Groups

At baseline, the absolute calorie intake reported by AN girls was comparable to controls (Table 3). Girls with AN had a greater percentage of total calories obtained from carbohydrates compared to controls ($p<0.001$), even though there was no difference in the reported absolute intake of carbohydrates. AN girls also consumed more fiber in their diet (p=0.002), and obtained a significantly greater percentage of total calories from fiber intake ($p<0.001$) than controls. At baseline, the reported absolute intake of fats (p=0.0002), including saturated fatty acid (SFA) and monounsaturated fatty acid (MUFA) was lower in girls with AN compared with controls ($p<0.0002$ and <0.001 respectively). The percentage of total calories obtained from total fat, SFA, MUFA ($p<0.001$ for all) and poly-unsaturated fatty acid (PUFA) (p=0.025) intake was lower in the AN group compared with controls. Protein intake did not differ between groups.

Comparisons of macronutrient intake in the AN-0 versus AN-1 groups at baseline are also presented in Table 3. The only difference in their dietary intake was that a greater percentage of total calories was obtained from protein in the AN-0 group (p=0.046).

Macronutrient Intake at Follow-up in the AN groups

At follow up, total caloric intake, total carbohydrate intake and percentage of total calories obtained from carbohydrate consumption did not differ significantly between AN-0 and AN-1 (Table 4). In contrast, the percentage of total calories obtained from fat consumption (total fats, PUFA, and MUFA) was significantly higher in AN-1 compared with AN-0 groups ($p\leq0.02$ for all). The percentage of total calories obtained from protein consumption was lower for AN-1 vs. AN-0 (p=0.001). Differences between AN-1 and AN-0 girls for consumption of percent calories from fat persisted after controlling for height change over the 6/12 month period, indicating no impact of change in height on this endpoint. Further, after controlling for baseline caloric intake, AN-0 had a trend towards lower fat (p=0.1) and

higher protein (p=0.1) consumption at follow-up, and consumed of a lower proportion of calories from fat (p=0.02) and a higher proportion of calories from protein (p=0.001). Similarly, AN-0 had a trend for a lower proportion of calories consumed from fat (p=0.06) and higher proportion of calories from proteins (p=0.01) compared to AN-1 after controlling for baseline fat intake and baseline protein intake, respectively. When examined as a continuous variable, percent calories obtained from fat at follow up predicted increases in BMI from baseline to 6 months (p=0.03). On analysis of the 34 AN participants who submitted their food diaries at 12 months only, AN-1 girls consumed more fat (p=0.01) and obtained a greater proportion of calories from fat (p=0.006) compared to the AN-0 group.

In subsequent analyses within AN girls based on menses recovery and weight gain, total caloric intake (1692.7±146.4 vs 2199.2±132.0 kcal), and protein intake (63.2±6.6 vs. 93.2±5.0 g) were lower in those who had recovered menses (p=0.048, and 0.004 respectively) vs. those who had not. There were no significant differences across groups for other nutrient intake.

Changes in Macronutrient Intake over 6/12 Months in the AN Groups

Girls with AN who gained weight (AN-1) had a significant increase in the percentage of total calories obtained from PUFA (0.5±0.12 vs. 0.07±0.08%, p=0.006) and trended to have a decrease in the percentage of total calories obtained from total dietary fiber (−0.11±0.17 vs. 0.24±0.06%, p=0.08) compared with those who did not gain weight (AN-0). The groups did not differ for changes in other nutrient intake over time.

Associations of Macronutrient Intake with Weight Gain

Within girls with AN, BMI at follow up correlated positively with the percentage of total calories obtained from total fat (r=0.41, p=0.005), MUFA (r=0.44, p=0.002), and PUFA (r=0.33, p=0.03) at 6–12 months, and inversely with the percentage of total calories obtained from carbohydrates (r=−0.32, p=0.03) and proteins (r=−0.33, p=0.03).

DISCUSSION

Data regarding the optimal choice of macronutrient intake that predicts weight gain in AN are currently limited. We examined the relationship of weight gain over a 6 to 12 month period in a sample of girls with AN with macronutrient intake at follow up and changes in macronutrient intake over time. To our knowledge our study is the first to evaluate macronutrient intake associated with weight gain in adolescent girls with AN. First, we demonstrate that participants with AN who have an at least 10% increase in BMI at 6/12 months obtain a higher percentage of total calories from fat consumption (total fat, MUFA and PUFA), at 6/12 months compared to those who do not gain weight. Further, AN participants who gain weight have a significant increase in the percentage of total calories obtained from PUFA consumption compared to those who do not gain weight.

In our study, adolescent girls with AN reported higher dietary fiber and lower fat intake compared to healthy controls, consistent with findings reported by Fernstrom et al and Misra et al (Fernstrom, et al., 1994; Misra, et al., 2006). Dietary fiber constituted 7.5% of the total carbohydrate intake and was consumed in higher quantities by AN girls compared to

controls. However, neither group consumed enough fiber to meet the recommended dietary intake (26 gm of fiber per day) (A. H. Association, 2015; Otten, Hellwig, & Meyers, 2005). Fat intake comprised 22% of the total caloric intake in the AN group, which was much lower than in controls (31%), consistent with the fat restricting behaviors typically exhibited by girls with AN (Drewnowski, et al., 1988; Fernstrom, et al., 1994; Misra, et al., 2006). Of interest, AN girls uniformly restricted all types of fats including SFA, MUFA, and PUFA, although PUFA intake only trended lower. We did not find any difference in protein intake between AN and control groups, similar to reports from previous studies (Fernstrom, et al., 1994; Misra, et al., 2006).

Of the macronutrients, fat intake was the major factor associated with weight gain. AN girls who gained weight (AN-1) obtained a significantly higher percentage of total calories from fat consumption compared to girls who did not gain weight (AN-0) (27% in AN-1 vs. 21% in AN-0). Importantly, there was no difference between AN-1 and AN-0 for their total caloric intake. During the study period the participants continued to be enrolled in treatment programs that included nutritional counseling. It is possible that those who did not gain weight over the time of the study were under closer surveillance in their treatment programs and had been recommended to increase in their caloric intake. This may have blunted observed differences across groups. The finding that the girls who gained weight derived a higher percentage of total calories from fat consumption than AN-0, despite consuming a similar amount of total calories, suggests that fat intake may be the major driver for weight gain in these girls. Consistent with these findings, weight-recovered adult women with AN who had treatment failure at one year of follow up had lower fat intake at the weight maintenance phase of their hospital stay suggesting the role of fat intake in maintaining recovery (Schebendach et al., 2008).

Intriguingly, in our study, the girls who gained weight obtained a higher percentage of total calories from fats such as PUFA and MUFA, and not from SFA, at follow-up suggesting close attention to specifics of fat intake. Particularly, an increase in intake of PUFA at follow-up was predictive of weight gain. Contrary to this finding, one study reported that a hypercaloric diet rich in varying fat contents (SFA vs. N-3 PUFA) did not show an effect on weight gain in anorexic women (Mauler et al., 2009). However, this study evaluated changes over a 5 week period in contrast to the 6–12 month period in our study, which might have contributed to the discrepancy. Additionally, certain foods such as nuts, seeds, and salmon that are rich in PUFA are also good sources of minerals such as zinc, which have been associated with weight gain in AN (Birmingham, Goldner, & Bakan, 1994). While the role of PUFA in weight gain AN is still unclear, it is important to note that in humans, PUFA is primarily derived from diet compared to other fatty acids that can be derived from other macronutrients (Ayton, 2004). Taken together, these data suggest that consuming a greater amount of fat may assist in weight gain during recovery from AN, even when total caloric intake and SFA intake are not significantly increased. Of note, it is also possible that the participants who gained weight were cognitively able to accept the addition of more fat to their diet, which resulted in increased fat intake at follow up.

We did not observe any differences in absolute carbohydrate or fiber intake for AN groups that did or did not gain weight at follow up. The girls who gained weight trended to have a

decrease in the percentage of total calories obtained from total dietary fiber intake over the follow-up period. Studies indicate that fiber intake reduces the rate of intestinal absorption and increases satiety (A. P. Association, 2000; Rigaud, Paycha, Meulemans, Merrouche, & Mignon, 1998) and it is possible that girls who did not gain weight were intending to consume food types that would enhance satiety.

Girls who gained weight also obtained a lower percentage of total calories from protein intake at 6/12 months follow up than the girls who did not gain weight. It is interesting to note that despite their higher energy intake as protein, no weight gain was observed in the AN-0 group, questioning the role of increased protein intake alone in weight gain. This observation supports the conclusion by Forbes et al., who suggested that there is no advantage to using a high protein diet in the rehabilitation of patients with AN (Forbes, 1984). Although, the effect of high protein diet on weight is controversial, it is possible that high dietary protein intake induces satiety and thermogenesis, and thus decreases caloric intake and prevents weight gain (Brehm & D'Alessio, 2008; Eisenstein, Roberts, Dallal, & Saltzman, 2002; Halton & Hu, 2004).

Importantly, girls with AN who also recovered menses with weight gain did not demonstrate increases in the percentage of calories consumed as fat or reductions in the percentage of calories consumed as fiber. Of concern, total caloric intake at 6/12 months was lower in AN who recovered menses, suggesting a volitional reduction in caloric intake following achievement of a key marker of recovery in girls with AN i.e. menses. Girls with AN in treatment programs are often not permitted to know their weight at follow-up for concerns of triggering behaviors that may lead to weight loss. However, menstrual recovery would indicate significant weight gain and may trigger a reduction in caloric intake. This suggests that close monitoring of caloric intake may be necessary at the time of menstrual recovery to avoid relapses.

Limitations of our study include those inherent to assessment of food records. Although the 4-day food diary correlates better with actual food intake than a 24-hour dietary recall (Morgan, 1978) the use of self-reported food records may have resulted in individuals over- or under-reporting their food consumption (de Castro, 2006). In general patients with AN are believed to over report food intake and a healthy population to underreport food intake (Hadigan, et al., 2000; Schebendach, Porter, Wolper, Walsh, & Mayer, 2012). However, Hadigan *et al.* have reported that despite the over reporting of caloric intake in AN, the reported macronutrient intake was similar to observed intake in women with AN, and concluded that dietary history may be a good tool to evaluate macronutrient and fat intake in this population (Hadigan, et al., 2000). Further, our data indicate very strong correlations between data obtained from dietary history and food records in adolescent girls with AN (Misra, et al., 2006), suggesting that food diaries are a reasonable strategy to assess nutrient intake in this population. Another factor that may have impacted our results is the possible tendency of AN girls who did not gain weight to over report caloric intake based on expectations of caregivers. This could have led to the lack of differences in reported caloric intake between groups that did or did not gain weight. Also, as alluded to earlier, our AN participants were recruited from the community through referrals from either health care providers or from treatment centers, and continued to receive treatment from their providers.

It is thus possible that differences between groups were blunted consequent to nutritional counseling provided to participants with AN who did not gain weight. Finally, caloric intake may have been impacted by differences in the nature and frequency of treatment received, and whether they were in residential or partial treatment during this period. Despite these issues and the tendency to over report, we show that girls with AN who did not gain weight consumed a lower percentage of total calories from fat ($p=0.02$) than those who did gain weight. Of note, food records were optional in the studies from which our data were extracted, raising the potential for bias. However, we found no difference in baseline characteristics in those who completed the food records at follow-up vs. those that did not.

Another study limitation is that factors other than food intake may impact weight gain, such as duration of illness, co-existence of psychiatric co-morbidities such as anxiety or depression, concomitant use of medications, and treatment compliance; these variables were not uniformly assessed. Also, participants were typically advised exercise restriction by their providers throughout the study period, which could have influenced weight gain.

Although our sample size compares well to earlier reports that have evaluated macronutrient intake using food records in AN (Misra, et al., 2006; Schebendach, et al., 2012), our study was not large enough to perform comparisons between weight restored patients who did and did not resume menses, which could be interesting. A major strength of our study is its prospective nature, which allowed us to observe the temporality of the association between macronutrient composition and weight gain.

In summary, our findings indicate that girls with AN who increase their fat intake and reduce their fiber intake relative to total intake experience weight gain over time. Prospective studies examining the effect of increased fat intake during recovery in AN, including specific nutrient analysis using objective measures of energy intake, such as doubly labeled water studies, are warranted to confirm these findings and to develop clinical guidelines for macronutrient intake for weight gain in AN.

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Table 1

Clinical Characteristics and Body Composition at Baseline in Girls with Anorexia Nervosa (AN) who gained ≥10% BMI (AN-1) vs. those that did not (AN-0) vs. Healthy Controls (HC)

	AN (n=45)	HC (n=45)	P (AN vs. HC)	AN-0 (n=23)	AN-1 (n=22)	P (AN-1 vs. AN-0)
Clinical Characteristics						
Age (y)	15.97±0.23	14.72±0.24	**0.0003**	15.83±0.30	16.12±0.34	0.53
Age of Menarche (y)	12.8±0.2	12.7±0.3	0.77	12.6±0.4	13.0±0.4	0.49
Height (cm)	164.6±1.0	163.2±1.0	0.33	163.1±1.5	166.2 ±1.4	0.14
Weight (kg)	45.3±0.9	54.2±1.1	**<0. 001**	44.6±1.4	45.9±1.0	0.46
Body Composition						
BMI (kg/m^2)	16.9±0.2	20.4±0.3	**<0.001**	16.9±0.3	16.8±0.3	0.74
BMI z-score	−1.93±0.18	0.15±0.11	**<0.001**	−1.87 ±0.28	−1.99±0.23	0.75
% Body fat (DXA)	16.8±0.8	27.2±0.8	**<0.001**	17.5±1.2	16.0±1.1	0.38
Lean Mass (kg)	36.5±0.7	38.6±0.8	0.052	35.5±1.1	37.5±1.0	0.20
Fat Mass (kg)	7.56±0.42	16.16±0.66	**<0.001**	7.67±0.63	7.45±0.55	0.79

Values presented as mean ± SEM. P values were obtained from Student's t test. AN: Anorexia Nervosa; HC; Healthy Controls; AN-0: AN subjects who did not gain ≥10% BMI at 6 or 12 months; AN-1: AN subjects who gained ≥10% BMI by 6 or 12 months.

Table 2

Body Composition in Girls with Anorexia Nervosa (AN) versus Controls, and in Girls with Anorexia Nervosa who gained ≥10% BMI (AN-1) vs. those that did not (AN-0) at 6/12 Months

	HC (n=45)	AN-0 (n=23)	AN-1 (n=22)	P (AN-1 vs. AN-0)	P (AN-1 vs. AN-0 vs. HC)
BMI (kg/m^2)	20.67±0.31	17.34±0.34	20.69±0.43	**<0.001**	**<0.001** *a,b*
BMI z-score	0.27±0.71	−1.59±0.24	−0.06±0.16	**<0.001**	**<0.001** *a,b*
% Body fat †	26.1 (22.4–32.4)	18.4 (14.9–23.2)	22.6 (19.7–22.3)	**0.005**	**<0.001** *a,b,c*
Lean mass (kg)	40.44±0.92	36.49±1.02	41.34±1.00	**0.002**	**0.007** *a,b*
Fat mass (kg) †	14.4 (12.2–18.6)	7.6 (6.0–11.7)	12.7 (10.4–14.6)	**0.001**	**<0.001** *a,b*

Values presented as mean±SEM or median (interquartile range). HC; Healthy Controls; AN-0: AN participants who did not gain ≥10% BMI at 6 or 12 months; AN-1: AN participants who gained ≥10% BMI by 6 or 12 months.

† Variables that were not distributed normally.

AN-0 and AN-1 groups were compared using the Student t-test or the Wilcoxon rank sum test depending on data distribution (parametric vs. non-parametric distributions respectively). Similarly, AN-0, AN-1 and HC groups were compared using ANOVA or the Kruskal-Wallis test depending on data distribution. The Tukey Kramer test (for parametric data) and the Steel-Dwass test (for non-parametric data) were used to control for multiple comparisons.

a: AN-0 VS AN-1, $p<0.05$,

b: AN-0 VS HC, $p<0.05$,

c: AN-1 VS HC, $p<0.05$

Table 3

Macronutrient Intake at Baseline in Girls with Anorexia Nervosa (AN) who gained ≥10% BMI (AN-1) vs. those that did not (AN-0) vs. Healthy Controls (HC)

	AN (n=45)	HC (n=45)	P (AN vs. HC)	AN-0 (n=23)	AN-1 (n=22)	P (AN-1 vs. AN-0)
Total Energy (kcal)	1884±1127	2001±73	0.38	1862±128	1907±189	0.84
Carbohydrates (g)	293.4±17.9	271.1±8.8	0.27	293.1±21.4	293.8±29.6	0.99
% Cal from Carbohydrates	62.9±1.26	54.9±1.11	**<0.0001**	64.6 (58.3–68.7)	61.7 (58.3–68.3)	0.65†
Fat (g)	47.3±4.1	70.2±4.4	**0.0002**	42.6±4.6	52.2±6.8	0.24
% Cal from Fat	21.8±1.12	30.9±1.1	**<0.0001**	20.2±1.8	23.4±1.6	0.18
Protein (g)	71.3±4.8	71.2±3.5	0.99	76.5±5.2	65.7±8.0	0.26
% Cal from Proteins	15.4±0.7	14.3±0.5	0.16	16.4 (14.0–18.9)	14.0 (12.0–17.5)	**0.046**†

Values presented as mean ± SEM or median (interquartile range). The Student t-test and Wilcoxon rank sum test were used for comparison of AN-0 and AN-1 groups for parametric and

†non-parametric data, respectively.

AN: Anorexia Nervosa; HC; Healthy Controls; AN-0: AN subjects who did not gain ≥10% BMI at 6 or 12 months; AN-1: AN subjects who gained ≥10% BMI by 6 or 12 months. % Cal: percent calories obtained from respective macronutrients.

Table 4

Macronutrient Intake at 6/12 Months in Girls with Anorexia Nervosa (AN) who gained ≥10% BMI (AN-1) vs. those that did not (AN-0) vs. Healthy Controls (HC)

	HC (n=45)	AN-0 (n=23)	AN-1 (n=22)	P (AN-1 vs. AN-0)	P (AN-1 vs. AN-0 vs. HC)
Total Energy (kcal)	1923.0±78.7	2029.7±113.6	2108.1±167.8	0.70	0.48
Carbohydrates (g)	262.3±11.5	309.0±16.2	306.4±25.3	0.93	0.06
% Cal from Carbohydrates	54.9±7.7	61.6±1.5	58.7±1.8	0.20	**0.004**^{b}
Fat (g)	63.8±3.5	48.5±5.9	63.8±6.9	0.10	0.07
% Cal from Fat	29.5±0.9	20.6±1.9	26.5±1.5	**0.02**	**<0.001**^{a,b}
Protein (g)	74.9±4.9	89.30±5.03	77.21±6.2	0.14	0.17
% Cal from Proteins	15.5±0.7	17.8±0.6	14.8±0.6	**0.001**	**0.03** ^{a}

Values presented as mean±SEM. HC; Healthy Controls; AN-0: AN participants who did not gain ≥10% BMI at 6 or 12 months; AN-1: AN participants who gained ≥10% BMI by 6 or 12 months.

AN-0 and AN-1 groups were compared using the Student t-test. AN-0, AN-1 and HC groups were compared using ANOVA, and the Tukey Kramer test was used to control for multiple comparisons.

^{a}: AN-0 VS AN-1, $p<0.05$,

^{b}: AN-0 VS HC, $p<0.05$,

^{c}: AN-1 VS HC, $p<0.05$