ORIGINAL RESEARCH PAPER

# Triiodothyronine (T3) and metabolic rate in adolescents with eating disorders: Is there a correlation?

D.L. Aschettino-Manevitz, R.M. Ornstein, W. Meyer Sterling, N. Kohn, and M. Fisher

Division of Adolescent Medicine, Steven and Alexandra Cohen Children's Medical Center, North Shore-Long Island Jewish Health System, New Hyde Park, NY, USA

**ABSTRACT. AIM:** *To examine the correlation between T3 and resting energy expenditure (REE) in adolescent patients with eating disorders (ED) to assess whether T3 can be used to predict metabolic rate suppression and recovery.* **METHODS:** *A retrospective chart review was performed on patients with ED (Anorexia Nervosa [AN], Bulimia Nervosa [BN], and Eating Disorder NOS [EDNOS]), aged 11-22 years, who had T3 and REE measured within 1 month (N=38 AN, 32 BN/EDNOS). REE was measured by indirect calorimetry (IC) and represented as the percentage of expected REE (%EREE) predicted by the Harris-Benedict equation. Pearson correlation coefficients were calculated to examine the relationship between T3 and %EREE and how each correlates with anthropometric data, laboratory values, and diagnosis.* **RESULTS:** *T3 was significantly correlated with %EREE in the AN group but not in the total population or BN/EDNOS group. In the total study population, T3 alone correlated significantly with weight, Body Mass Index (BMI), BMI percentile, %Ideal Body Weight (%IBW), %Maximum Weight Lost (%MWL), LH, and estradiol. In the AN group, T3 and %EREE both correlated with BMI, BMI percentile, LH, and estradiol; however, only T3 correlated with %IBW and %MWL. In the BN/EDNOS group, T3 correlated with BMI, BMI percentile, %IBW, and estradiol while %EREE correlated with none.* **CONCLUSION:** *In patients with AN, T3 correlated significantly with markers of malnutrition and %EREE and may serve as a surrogate measure when IC is unavailable. Following T3 during treatment of AN may assist clinicians in assessing metabolic suppression and recovery and help guide caloric prescriptions and goal weights.*

*(Eat. Weight Disord. 17: e252-e258, 2012). ©2012, Editrice Kurtis*



## INTRODUCTION

Eating disorders significantly impact the nutritional status of adolescents at a critical time in physical and psychosocial development. They rank as the third most common chronic illness in adolescent females, with an incidence up to 5% (1). Malnutrition as a consequence of an imbalance between caloric intake compared to energy expenditure can seriously affect normal endocrine function with resultant diminished metabolic rates. The body adapts to lack of energy intake (in the form of kilocalories) by reducing all non-essential functions to conserve energy in order to support the most vital functions. In states of starvation, in the absence of adequate carbohydrate and calcium intake, the body will break down lean muscle mass, including heart tissue and bone, to provide the necessary substrates to feed the brain and vital organs. Heart rate, body temperature, and gastrointestinal transit time all decrease in malnutrition, and amenorrhea is common. Many of these adaptations are mediated through changes in thyroid function (2).

Malnutrition secondary to anorexia nervosa (AN) alters Hypothalamic-Pituitary-Thyroid (HPT) axis function in an adaptive response to starvation (3). Changes in enzyme activity can be seen even with modest medical illness or fasting, resulting in reduced serum T3 and increased reverse T3 (rT3). In multiple studies, T3 has been shown to decrease with caloric restriction to levels below normal in patients with AN and improve with refeeding and weight gain. In one study, by Tamai et al., women with AN were found to have significantly lower serum total and free T4, total and free T3, thyroid stimulating hormone (TSH), thyroid binding globulin (TBG) and thyroxine binding pre-albumin (TBPA) val-

*First online ahead of publication November 26, 2012 as DOI: 10.3275/8756*

**Key words:**
*Adolescents, eating disorders, anorexia nervosa, metabolism, thyroid, triiodothyronine(T3), metabolic rate.*

**Correspondence to:**
*Martin Fisher, MD, Division of Adolescent Medicine, Steven and Alexandra Cohen Children's Medical Center, North Shore-Long Island Jewish Health System, 410 Lakeville Road, Suite 108, New Hyde Park, NY 11042, USA.*
*E-mail: MFisher2@NSHS.edu*

**Received:** *February 19, 2012*
**Accepted:** *November 12, 2012*

ues than controls and rT3 levels higher than controls. Patients restudied after weight restoration showed significant increases in T4, total and free T3, TSH, TBG and TBPA levels, decreased rT3 levels, and no change in mean free T4 levels (4). In a study by Croxson et al., comparing patients with AN with euthyroid control subjects, serum total T3, serum-adjusted T4, and Achilles tendon relaxation time were significantly lower in the AN group compared to the control subjects (5). In patients with significant weight gain from refeeding, the changes in HPT function were reversed and serum T3 rose. In another study, by Misra et al., subjects with AN were compared to control subjects and serum total T3 was significantly lower in the AN patients compared to the controls (6).

Alterations in metabolism as a result of caloric restriction are not limited to patients with AN, and have even been shown in obese patients after caloric restriction. In a study by Marine in 1991, obese adults were given a diet of 320 kcal per day for up to 13 weeks (7). In these patients, baseline serum T3 levels were found to initially be relatively elevated, in the high normal range, and were decreased after caloric restriction. The data suggest that alterations of thyroid hormone metabolism by peripheral tissues during caloric deprivation in a protein sparing fast result in decreased serum T3 levels.

It is thought that thyroid hormone influences body weight by regulating resting energy expenditure (REE), although the exact mechanism for the thermogenic effect is unknown (3). Low levels of thyroid hormone decrease REE and high levels increase REE (8). Approximately 20-25% of REE is thyroid hormone-dependent such that small changes in thyroid hormone levels have a significant effect on REE. For example, an increase of 0.5-1 mU/L in serum TSH results in a reduction of REE by 75-150 kcal/d (9). While there have been studies documenting decreased T3 levels in malnourished states and increases with refeeding, to our knowledge, there have not been any studies that have examined the correlation between T3 and measured REE.

REE can be measured using indirect calorimetry (IC), a noninvasive technique that has been utilized in nutritional management of patients with eating disorders, obesity, and other illnesses where energy requirements often vary from predicted values calculated by the Harris-Benedict Equation (HBE) (10) which is based on height, weight, sex, and gender. In a study performed by Schebendach et al., the REE of patients with AN and BN was assessed using IC and found to be markedly lower than the predicted REE in both groups (11). IC has also been studied in various hospitalized patient populations and has consistently been shown to differ from the HBE predictions, leading practitioners to consider IC to be the gold standard for assessment of REE in hospitalized patients (12). Comparing these two values and expressing them as a percentage of expected REE (%EREE) has come to be a useful tool in quantifying metabolic suppression and recovery.

In the eating disorder population, REE has been measured by IC throughout the process of nutritional rehabilitation. In a prospective study by Schebendach et al., 50 hospitalized patients with AN had REE measured at baseline and every 2 weeks during hospitalization using IC (13). When expressed as a percent of predicted, REE increased from 72% of predicted to 94.1% of predicted by 6 weeks, demonstrating metabolic recovery. Researchers also measured T3 levels and assessed postprandial energy expenditure. It was theorized that T3 levels may play a role in post-prandial thermogenesis; however, the data did not correlate significantly. There was, however, a consistent increase in T3 levels with weight gain (13).

We sought to examine the correlation between T3 and REE as measured by IC in adolescents with eating disorders in inpatient and outpatient settings. The goal was to determine whether T3 could be used to predict metabolic rate suppression and recovery. It was hypothesized that because T3 and REE are both known to be suppressed in malnutrition, T3 values would directly correlate with measured REE. As IC is not readily available in many clinical sites, and is often not covered by insurance, it was theorized that T3 could potentially serve as a useful tool to monitor patients during refeeding and maintenance.

## METHODS

*Subjects*

An institutional review board approved, retrospective chart review was performed. Charts of inpatients and outpatients in an eating disorders program who had IC studies performed between January 1, 2006 and June 30, 2008 were reviewed. All adolescent male and female patients with a diagnosis of anorexia nervosa (AN), bulimia nervosa (BN) or eating disorder not otherwise specified (EDNOS) who had IC were eligible for inclusion. Eating disorder diagnoses were determined by a multidisciplinary team with input from treating physicians,

nutritionists, nurses, psychiatrists, and social workers (14). Exclusion criteria included conditions which may alter metabolic rate such as: pregnancy, malignancy, thyroid disease, or other chronic illnesses (i.e. inflammatory bowel disease, diabetes mellitus, and renal disease). Patients who had T3 values within one month of the metabolic study were included. This one-month time period was selected to limit the amount of possible change in weight and nutritional status between the T3 and IC measures. Given that all patients were involved in treatment of their eating disorders, we expected this change to be in the direction of a weight increase in patients with AN and reduction in malnutrition in general.

Subjects were identified using three sources: a computer generated list of patients admitted to the inpatient eating disorder program, the log books of inpatient IC tests that were performed, and a list of all IC tests performed in the outpatient clinic. Most patients treated in the eating disorders program are treated as outpatients; those who are more severely malnourished generally start in the inpatient unit and then move from the inpatient unit to a day hospital program to outpatient care as their condition improves. Patients who were being treated on the inpatient unit had their IC test on one machine; patients who were being treated in the day program or as outpatients had their IC measured on a second machine. Machines were of similar make and model and IC tests were conducted using the same procedure in both locations.

*Measures*

Laboratory. All quantitative serum T3 levels were measured utilizing radioimmunoassay (RIA) by the North Shore-Long Island Jewish Health System Laboratory or by Quest Diagnostics Laboratory. Where available, T4, free T4, TSH, luteinizing hormone (LH), and estradiol levels were also recorded. Length of time between laboratory testing and IC measures were captured to evaluate if this variable impacted the correlations.

Indirect Calorimetry. REE was measured using an open-circuit, mixed chamber collection, computerized IC system (Datex Deltra-Trac II, Sensor Medics, Anaheim, California) after an overnight fast. Patients were instructed to refrain from eating and drinking from midnight until the examination was performed in the morning. Outpatients were told not to exercise for 24 hours prior to testing. Inpatients were restricted from exercise throughout their hospitalization and were brought to the study in a wheelchair to minimize energy expenditure. An additional 15 minute rest period in the supine position was implemented prior to testing. Patients were instructed to remain awake and in a supine position throughout the test, which lasted approximately 25 minutes. Measured resting energy expenditures (MREE) were compared to the resting energy values predicted by the Harris-Benedict Equation (HBREE) (10). Values were then expressed as a %EREE.

Anthropometric Assessment. Anthropometric and diagnostic data included: gender, age, height, weight, body mass index (BMI), BMI percentile, ideal body weight (IBW), %IBW, diagnosis, and treatment level status (inpatient, day hospital, outpatient). IBW was defined as the median weight for height and gender using the National Center for Health Statistics percentiles (15). As available, we recorded maximum premorbid weight, time since maximum weight, %maximum weight lost (%MWL), total weight lost, and duration of weight loss.

*Statistics*

Based on a power analysis, it was calculated that a sample size of 40 patients was required to yield 80% power to detect a correlation between REE and T3 of 0.435 or higher at the 0.05 significance level. All analyses were carried out separately for each of the three distinct diagnoses: AN, BN, and EDNOS. As there were only 5 subjects with BN and they did not appear to be appreciably different from the EDNOS group, their data was combined for purposes of statistical analysis.

The association between T3 and %EREE was examined by calculating the Pearson correlation coefficient. Measurements of T3 and MREE were not always performed on the same day. To verify that the time between measurements did not affect the correlation, the partial correlation of T3 and %EREE, adjusted for time, was calculated.

Associations between both T3 and %EREE and categorical baseline variables (gender, treatment status) were examined using the two sample t-test. Associations between both T3 and %EREE and continuous factors (age, BMI, BMI percentile, %IBW, %MWL, Duration of Loss) were examined by calculating Pearson correlation coefficients. For T3, the log transformation was used to better meet the assumptions (normality, homoscedasticity) required for parametric models. As the Pearson correlation coefficient values for T3 and the log of T3 did not differ qualitatively (with the exception of one minor difference in the multivariate models to be discussed later), T3 values are presented for ease of interpretation for the

**TABLE 1**
Baseline demographics by diagnosis.

| Total Subjects N=70 | Anorexia Nervosa, N=38, N (%) | Eating Disorder not otherwise specified, N=27, N (%) | Bulimia Nervosa N=5, N (%) |
|---|---|---|---|
| Gender | | | |
| Female | 37 (97.4%) | 21 (77.8%) | 5 (100%) |
| Male | 1 (2.6%) | 6 (22.2%) | 0 (0.0%) |
| Status | | | |
| Inpatient | 20 (52.6%) | 9 (33.3%) | 0 (0.0%) |
| Day Program | 12 (31.6%) | 6 (22.2%) | 4 (80.0%) |
| Outpatient | 6 (15.8%) | 12 (44.4%) | 1 (20.0%) |

clinician. In order to further examine the association between T3 and %EREE, and how other factors might affect that association, two linear regression models were examined. In the first model, T3 was the dependent variable and %EREE, BMI, and %MWL were the independent variables. In the second model, %EREE was the dependent variable and T3, BMI, and %MWL were the independent variables.

## RESULTS

*Anthropometric Status, Energy Expenditure and Laboratory Status*

In total, 361 charts were reviewed, yielding 70 qualified patients with 86 pairs of T3 and IC, taking into consideration multiple IC/T3 pairs for some patients and excluding duplication in others. The demographics of these subjects by diagnosis, gender and status are summarized in Table 1. Table 2 demonstrates baseline anthropometrics, IC results, and laboratory measures for all study subjects, as well as by group (AN and BN/EDNOS)

The mean REE did not differ significantly between patients with AN (73.6%) and those with BN/EDNOS (74.9%). Mean values of T3 , LH, and estradiol were all at or below the lowest range of normal values, as expected for patients with eating disorders, and were all lower for patients with AN than for those with BN/EDNOS. By definition of our inclusion/exclusion criteria, TSH, T4 and free T4 were in the normal range, excluding patients



**TABLE 2**
Demographics by diagnosis: continuous variables.

| | All Patients | | Anorexia Nervosa | | BN or EDNOS | |
|---|---|---|---|---|---|---|
| | N | Mean (SD) | N | Mean (SD) | N | Mean (SD) |
| **Anthropometric Status** | | | | | | |
| Age (yrs) | 70 | 16.3 (2.2) | 38 | 16.1 (2.2) | 32 | 16.4 (2.2) |
| Height (cm) | 70 | 162.1 (8.6) | 38 | 161.9 (8.4) | 32 | 162.5 (8.9) |
| Weight (kg) | 70 | 46.5 (10.3) | 38 | 42.4 (7.6) | 32 | 51.3 (11.1) |
| BMI | 70 | 17.5 (3.1) | 38 | 16.1 (2.2) | 32 | 19.2 (3.2) |
| BMI Percentile | 64 | 18.1 (24.9) | 35 | 7.9 (14.4) | 29 | 30.5 (29.3) |
| IBW (kg) | 42 | 54.4 (7.6) | 20 | 54.2 (8.3) | 22 | 54.6 (7.2) |
| %IBW | 69 | 84.7 (14.6) | 37 | 77.1 (10.7) | 32 | 93.6 (13.7) |
| Max Weight (kg) | 57 | 61.7 (20.5) | 28 | 54.5 (14.4) | 29 | 68.6 (23.2) |
| Initial Weight (kg) | 65 | 44.3 (12.2) | 34 | 38.7 (7.9) | 31 | 50.4 (13.2) |
| %Max Weight Lost | 57 | 23.5 (13.3) | 28 | 24.3 (13.3) | 29 | 22.6 (13.4) |
| Weight Loss Duration (months) | 54 | 14.9 (14.0) | 27 | 12.3 (10.3) | 27 | 17.5 (16.7) |
| **Energy Expenditure by Indirect Calorimetry** | | | | | | |
| MREE (Kcal/day) | 70 | 993.7 (186.6) | 38 | 953.9 (162.8) | 32 | 1040.9 (204.0) |
| HBREE (Kcal/day) | 70 | 1338.0 (140.3) | 38 | 1292.2 (95.2) | 32 | 1392.4 (165.4) |
| %EREE | 70 | 74.2 (10.8) | 38 | 73.6 (9.8) | 32 | 74.9 (12.0) |
| **Laboratory Measures** | | | | | | |
| T3 (ng/dl) | 70 | 80.3 (29.8) | 38 | 69.1 (22.4) | 32 | 93.6 (32.2) |
| TSH (uIU/ml) | 66 | 1.67 (0.78) | 37 | 1.80 (0.83) | 29 | 1.50 (0.684) |
| T4 serum (ng/dl) | 51 | 6.49 (1.17) | 27 | 6.17 (1.01) | 24 | 6.84 (1.27) |
| Free T4 (ng/dl) | 35 | 1.03 (0.30) | 16 | 0.997 (0.232) | 19 | 1.065 (0.357) |
| LH (mIU/ml) | 47 | 2.91 (4.28) | 26 | 1.33 (1.99) | 21 | 4.88 (5.46) |
| Estradiol (pg/ml) | 46 | 24.4 (14.3) | 28 | 19.1 (8.3) | 18 | 32.7 (17.6) |
| **Days Between Labs and Energy** | 70 | 10.6 (7.7) | 38 | 11.0 (7.3) | 32 | 10.1 (8.2) |

BMI: Body Mass Index; IBW: Ideal Body Weight; MREE: Measured Resting Energy Expenditure; HBREE: Harris-Benedict Resting Energy Expenditure; %EREE: Percentage of Expected Resting Energy Expenditure.

**TABLE 3**
Pearson correlation coefficients for continuous variables.

| | All Patients | | | | Anorexia Nervosa Subgroup | | | | BN/EDNOS Subgroup | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | T3 | | %EREE | | T3 | | %EREE | | T3 | | %EREE | |
| **Factor** | **r** | **p** | **r** | **p** | **r** | **p** | **r** | **p** | **r** | **p** | **r** | **p** |
| Age (yrs) | -0.07 | 0.592 | -0.07 | 0.590 | 0.17 | 0.308 | 0.14 | 0.411 | -0.06 | 0.756 | -0.27 | 0.129 |
| Weight (kg) | **0.41** | **<0.001** | 0.15 | 0.221 | 0.26 | 0.117 | **0.40** | **0.013** | 0.30 | 0.092 | -0.03 | 0.845 |
| BMI | **0.55** | **<0.001** | 0.15 | 0.202 | **0.44** | **0.005** | **0.43** | **0.007** | **0.43** | **0.014** | -0.05 | 0.809 |
| BMI %tile | **0.56** | **<0.001** | 0.13 | 0.324 | **0.39** | **0.019** | **0.45** | **0.007** | **0.49** | **0.007** | -0.06 | 0.760 |
| %IBW (kg) | **0.59** | **<0.001** | 0.18 | 0.136 | **0.44** | **0.007** | 0.26 | 0.116 | **0.47** | **0.006** | 0.09 | 0.609 |
| %Max Weight Lost | **-0.36** | **0.006** | 0.04 | 0.793 | **-0.45** | **0.015** | -0.04 | 0.822 | -0.32 | 0.092 | 0.10 | 0.608 |
| Loss Duration (months) | 0.13 | 0.349 | -0.10 | 0.466 | -0.19 | 0.353 | -0.33 | 0.093 | 0.17 | 0.398 | -0.03 | 0.892 |
| TSH | -0.22 | 0.074 | 0.07 | 0.557 | -0.18 | 0.299 | 0.16 | 0.343 | -0.16 | 0.402 | -0.01 | 0.966 |
| T4 serum | **0.52** | **<0.001** | 0.17 | 0.223 | **0.54** | **0.004** | 0.25 | 0.202 | **0.42** | **0.043** | 0.04 | 0.859 |
| Free T4 | 0.06 | 0.356 | 0.05 | 0.765 | -0.14 | 0.616 | -0.05 | 0.850 | 0.24 | 0.313 | 0.11 | 0.648 |
| LH | **0.50** | **<0.001** | -0.13 | 0.383 | **0.66** | **<0.001** | **0.46** | **0.019** | 0.29 | 0.207 | -0.38 | 0.087 |
| Estradiol | **0.75** | **<0.001** | 0.29 | 0.053 | **0.64** | **<0.001** | **0.44** | **0.019** | **0.72** | **<0.001** | 0.18 | 0.466 |

BMI: Body Mass Index; IBW: Ideal Body Weight; %EREE: Percentage of Expected Resting Energy Expenditure.



with thyroid conditions that might affect our measures of metabolic rate. Mean number of days between the time that the laboratory tests were drawn and the IC was performed was 10.6 days (SD 7.7); this did not differ significantly for those with AN vs those with BN/EDNOS.

*Correlates with T3 and Resting Energy Expenditure*

Pearson correlation coefficients were determined for each of the anthropometric and laboratory parameters with respect to T3 and %EREE, as shown in Table 3 for all patients, as well as the subgroups. There were no statistically significant correlations between %EREE and any of the anthropometric or laboratory parameters for the entire study population. However, T3 did correlate significantly with weight, BMI, BMI percentile, %IBW, %MWL, T4, LH, and estradiol for the entire study population. When patients with AN were examined separately from those with BN/EDNOS, several significant correlations were found. T3 correlated with multiple weight parameters (BMI, BMI percentile, %IBW, %MWL) and laboratory values (T4, LH, estradiol). Similarly, %EREE correlated significantly with several weight (weight, BMI, BMI percentile) and laboratory (LH, estradiol) variables. In the patients with BN/EDNOS, several of the weight (BMI, BMI percentile, %IBW) and laboratory (T4, estradiol) values were significantly correlated with T3 while none of the parameters were correlated with %EREE.

Table 4 demonstrates the Pearson correlation coefficients for T3 and %EREE for the total study population and the two subgroups. For the entire cohort, T3 did not correlate with %EREE. However, when the population was subdivided, T3 did correlate significantly with %EREE (r=0.35, p=0.034) in the AN subgroup but not in the BN/EDNOS group. Pearson partial correlation coefficients adjusting for days between measurements for the entire study population and the separate subgroups were also calculated (Table 4). As the partial correlation did not differ qualitatively from the standard correlation, it was determined that the time interval between measurements did not affect the relationship.

*Multivariate Linear Regression Models*

The statistically significant anthropometric and energy correlations were entered into two

**TABLE 4**
The Pearson Correlation Coefficients (standard and partial) for the T3 with %EREE by diagnosis.

| | | Pearson Correlation Coefficient | | Partial Correlation (adjusted for days between measurements) | |
|---|---|---|---|---|---|
| **Diagnosis** | **n** | **r** | **p-value** | **r** | **p-value** |
| All Patients | 70 | 0.13 | 0.277 | 0.14 | 0.247 |
| Anorexia Nervosa | 38 | **0.35** | **0.034** | **0.36** | **0.029** |
| BN/EDNOS | 32 | -0.03 | 0.853 | -0.03 | 0.879 |

BN: Bulimia Nervosa; EDNOS: Eating Disorder Not Otherwise Specified; %EREE: Percentage of Expected Resting Energy Expenditure.

multivariate linear regression models. The first model utilized T3 as the dependent variable and the second model utilized %EREE as the dependent variable. In both models, since BMI, BMI percentile, and %IBW were so highly correlated with each other (with r values of 0.83 to 0.91, p<0.001), BMI was used alone to represent these three variables. Results of the two models are presented in Table 5. In the first model, with T3 as the dependent variable, $R^2$ for all variables in the model was 0.38, %MWL was significant (p=0.016), but neither the BMI, as an indicator of current weight status, nor the %EREE, remained as significant correlates. In the second model, with the %EREE as the dependent variable, the $R^2$ for all variables was 0.35 and only BMI remained significant (p=0.037). These results are slightly different than the calculations using log of T3, where BMI was not significant (p=0.060).

## DISCUSSION

This study found that T3 correlated significantly with parameters of weight, BMI, BMI percentile, %IBW, %MWL, T4, LH, and estradiol for the entire study population, while %EREE did not correlate with any continuous variables including T3. Thus, T3 may be a better indicator of clinical status in adolescents with eating disorders than %EREE. It was also found that when the entire cohort was separated by diagnosis, the AN subgroup demonstrated a significant correlation between T3 and %EREE. In the AN patients, it appears that although both T3 and %EREE vary with markers of malnutrition, their relationship is not linear and likely reflects a combination of factors. The mean T3 and mean %EREE were both low for AN subjects, as might be expected. BMI and BMI percentile correlated similarly with T3 and %EREE. Interestingly, in the AN patients, T3 correlated more strongly with the anthropometric measurements than did %EREE. It was surprising that %IBW was positively correlated with T3, but not with %EREE. Similarly, %MWL correlated significantly with T3 but not with %EREE. Additionally, T3 correlated well with other laboratory values typically affected by malnutrition, such as LH and estradiol, much more so than %EREE. This may have been the case because levels of these hormones depend more closely on the same substrates of nutrition than does REE, or perhaps the differences lie in mechanisms of the metabolic response to refeeding that are still unknown.

The prior study by Schebendach et al. (11), in hospitalized patients with AN, investigated post-prandial energy expenditure and the possible role of T3 in post-prandial thermogenesis, while this study examined pre-prandial REE and how T3 correlated with %EREE, as well as anthropometric and laboratory parameters. Our study was also not limited to inpatient AN patients and included patients with EDNOS and BN in inpatient, day hospital, and outpatient settings. Like this earlier study, we found that T3 and %EREE increased with weight gain in the few patients with multiple T3 and %EREE sets, although we did not have enough data for full statistical analysis. We also found that the T3 and %EREE values were lowest in inpatients, higher in day hospital patients, and highest in outpatients, likely reflecting the usual progression in clinical status with weight gain in treatment.

Unlike the AN patients, in the more heterogeneous BN/EDNOS subjects, %EREE and T3 did not correlate. Additionally, %EREE did not correlate significantly with any of the factors in the BN/EDNOS subgroup. However, T3 did correlate with BMI, BMI percentile, %IBW, and estradiol, which may demonstrate the complexity of resting metabolism in this diverse population. It appears that resting energy expenditure, as measured by %EREE, is complex and depends on other variables beyond anthropometric measures. For example, in BN patients of normal weight (defined as ≥90% IBW using US National Center for Health Statistics data) (15), %EREE is decreased and the pathophysiology of metabolic suppression and amenorrhea in this population is not yet completely understood. Anecdotally, many patients diagnosed with EDNOS, who may be of normal weight but have lost a large percentage of their maximum weight, are as hypometabolic as AN patients by %EREE, despite normal to above normal BMI or %IBW. These results are sup-

**TABLE 5**
Multivariate Linear Regression Models for AN.

| | **T3 as Dependent Variable, $R^2$=0.38** |
|---|---|
| Independent Factor | p-value |
| %EREE | 0.059 |
| BMI | 0.610 |
| %Max Weight Lost | **0.016** |
| | **%EREE as Dependent Variable, $R^2$=0.35** |
| Independent Factor | p-value |
| T3 | 0.059 |
| BMI | **0.037** |
| %Max Weight Lost | 0.320 |

BMI: Body Mass Index; %EREE: Percentage of Expected Resting Energy Expenditure.

ported by a prior study conducted out of this division, which showed a suppression in REE in an eating disorder population despite being 90-130% IBW (16). T3 may be more directly related to measures of weight, but its utility to predict metabolism is unclear in this population as it did not correlate with %EREE.

The greatest limitation of this study is its retrospective nature. T3 and REE were not measured in most cases on the same day, possibly allowing for changes in nutritional status to occur between the measurements. Although our inclusion criteria limited the time lapse between laboratory and IC measurements to less than one month, the average interval was 10.6 days. As the Pearson partial correlation coefficients adjusting for days between measurements did not differ qualitatively from the standard correlation, it was determined that the time interval between measurements did not affect the relationship between T3 and %EREE. A prospective study in which laboratory and IC testing were performed on the same day would be beneficial to further elucidate the association between T3 and %EREE in eating disorder patients. In addition, it would be interesting to further investigate the concept of %MWL in predicting clinical status in eating disorder patients as it appears to be the best predictor of T3 in the multivariate models in the AN population.

We demonstrated significant correlations between T3 and %EREE, as well as other markers of malnutrition, in adolescent patients with AN. Therefore, in this group of eating disorder patients, T3 may serve as a surrogate measure for REE when IC is not available. T3 is strongly associated with other clinical indicators of malnutrition while %EREE is not, when considering all ED diagnoses. Following T3 during treatment of AN may assist clinicians in assessing metabolic suppression and recovery and help guide determination of caloric prescriptions and goal weights.

*Implications and Contribution*

This study looks directly at the utility of following T3 in adolescent eating disorder patients during treatment and evaluating how it relates to the resting energy expenditure as measured by indirect calorimetry, and finds a significant association with many anthropometric and laboratory parameters even when %EREE does not.

## REFERENCES


1. Golden NH, Katzman DK, Kreipe RE, et al. Eating Disorders in Adolescents: Position Paper of the Society for Adolescent Medicine. J Adolesc Health 2003; 33: 496-503.
2. Langton JE, Brent, GA. Nonthyroidal illness syndrome evaluation of thyroid function in sick patients. Endocrinol Metab Clin North Am 2002; 31: 159-72
3. Silva JE. Thyroid hormone control of thermogenesis and energy balance. Thyroid 1995; 5: 481-92.
4. Tamai H, Mori K, Matsubayashi S, et al. Hypothalamic-pituitary-thyroidal dysfunctions in anorexia nervosa. Psychother Psychosom 1986; 46: 127-31.
5. Croxson M, Ibbertson H. Low serum triiodothyronine (T3) and hypothyroidism in anorexia nervosa. J Clin Endocrinol Metab 1977; 44: 167-74.
6. Misra M, Miller KK, Tsai P, et al. Uncoupling of cardiovascular risk markers in adolescent girls with anorexia nervosa. J Pediatr 2006; 149: 763-9.
7. Marine N. Dietary restriction on serum thyroid hormone levels. Am J Med Sci 1991; 301: 310-3.
8. Douyon L, Schteingart D. Effect of obesity and starvation on thyroid hormone, growth hormone, and cortisol secretion. Endocrinol Metab Clin North Am 2002; 31: 173-89.
9. Al-Adsani H, Hoffer L, Silva JE. Resting energy expenditure is sensitive to small dose changes in patients on chronic thyroid hormone replacement. J Clin Endocrinol Metab 1997; 82: 1118-25.
10. Schbendach J. The use of indirect calorimetry in the clinical management of adolescents with nutritional disorders. Adolesc Med 2003; 14: 77-85.
11. Schebendach J, Golden NH, Jacobson MS, et al. Indirect calorimetry in the nutritional management of eating disorders. Int J Eat Disord 1995; 17: 59-66.
12. Boullata J, Williams J, Cottrell F, et al. Accurate determination of energy needs in hospitalized patients. J Am Diet Assoc 2007; 107: 393-401.
13. Schebendach JE, Golden NH, Jacobson MS, et al. The metabolic responses to starvation and refeeding in adolescents with anorexia nervosa. Ann NY Acad Sci 1997; 817: 110-9.
14. American Psychiatric Association. Diagnostics and Statistical Manual of Mental Disorders, 4th Ed. Washington, DC, APA, 1994.
15. Hamill PVV, Johnston FE, Lemeshow S. Height and weight of youths 12-17 years: United States National Center for Health Statistics. Vital and Health Statistics Series 1973 (Series 11); 124: 73-1606.
16. Meyer Sterling W, Golden N, Jacobson M, et al. Metabolic assessment of menstruating and non-menstruating normal weight adolescents. Int J Eat Disord 2009; 42: 658-63.