Randomized Trial Reveals that Physical Activity and Energy Expenditure are Associated with Weight and Body Composition after RYGB

Elvis Alvarez Carnero1, Gabriel S. Dubis2, Kazanna C. Hames3, John M. Jakicic4, Joseph A. Houmard2, Paul M. Coen3,4, and Bret H. Goodpaster3

Objective: This study investigated the associations of both physical activity time (PA) and energy expenditure (EE) with weight and fat mass (FM) loss in patients following Roux-en-Y gastric bypass (RYGB) surgery.

Methods: Ninety-six nondiabetic patients were included in this analysis. Post-RYGB patients were randomized in one of two treatments: A 6-month exercise training program (RYGB+EX) or lifestyle educational classes (RYGB). Body composition was assessed by dual-energy X-ray absorptiometry and computed tomography. Components of PA and EE were quantified by a multisensory device. Dose-response relationships of both PA and EE with weight loss and body composition were explored according to quartiles of change in steps per day.

Results: Patients in the highest quartiles of steps per day change lost more FM (3rd = −19.5 kg and 4th = −22.7 kg, P < 0.05) and abdominal adipose tissue (4th = −313 cm², P < 0.05), maintained skeletal muscle mass (3rd = −3.1 cm² and 4th = −4.5 cm², P < 0.05), and had greater reductions in resting metabolic rate. Decreases in sedentary EE and increases in light EE and age were significant predictors of both Δweight and ΔFM (R² = 73.8% and R² = 70.6%, respectively).

Conclusions: Nondiabetic patients who perform higher, yet still modest, amounts of PA following RYGB have greater energy deficits and lose more weight and FM, while maintaining higher skeletal muscle mass.

Introduction

Roux-en-Y gastric bypass (RYGB) surgery is generally an effective and safe treatment option to reduce weight in patients with severe obesity (1). The degree of weight loss, however, varies considerably among patients (2). While bariatric surgery reduces energy intake and absorption, it is not clear whether alterations in energy expenditure (EE) contribute to the variability in weight loss and incidence of weight regain (3,4).

Targeting total daily energy expenditure (TDEE) compartments is a strategy that may be useful to reduce body weight (3,5). Physical activity EE (PAEE), resting metabolic rate (RMR), and thermic effect of food (TEF) are the primary components of TDEE, and their importance for the treatment of obesity has been previously described (3,5). While physical activity (PA) interventions increase PAEE, RMR and TEF are more difficult to target. Indeed, the decrease in RMR has been well described as an adaptive thermogenesis in response to caloric restriction (6) and has been postulated to contribute to weight management (7). Additionally, and contrary to a commonly held belief, evidence suggests that exercise training also reduces RMR (8). In accord with this, DeLany et al. reported a positive relationship between an increase in steps per day and a...
decrease in RMR among subjects with severe obesity (9). While RMR is the largest component of TDEE and is potentially affected by exercise or PA, the relative contribution and interaction of resting and activity-related components of EE during regulation of body weight following RYGB surgery have received very little attention. Further investigation of EE regulation following bariatric surgery is needed to understand the variability in weight loss.

Exercise after RYGB has been suggested to promote greater weight loss (10,11) and can improve cardiometabolic risk factors, independently of changes in body weight or body composition (12). However, potential effects of a structured exercise program on weight loss and EE are difficult to tease apart from the effects on nonexercise physical activity (NEPA) and sedentary time (13), which may increase after RYGB (14). Objectively quantifying components of daily PA (light, moderate, and vigorous PA and sedentary behaviors) and EE (RMR, TEF, and PAEE) during an exercise training program following bariatric surgery could help elucidate how they could play a role in weight loss. Although accurate and valid measurements of total daily PA (TDPA) can be made using wearable monitors that capture nearly 24 hours of daily activity over several weeks (15,16), these approaches have not been employed to quantify PA and EE during exercise interventions following RYGB (17).

To examine the relationships between TDPA, TDEE, exercise training, sedentary time, RMR, and weight loss, we conducted a secondary analysis of data collected from a randomized controlled exercise trial following RYGB, i.e., exercise versus nonexercise control. First, we determined the impact of an exercise intervention on components of resting and activity-related EE, NEPA, and sedentary time. We then determined weight loss and changes in body composition (body fat and lean body mass) and components of EE according to change in PA (steps/day) in a dose-response fashion, independently of group assignment. Finally, we explored TDEE and TDPA components as plausible predictors of weight and fat mass (FM) changes.

Methods
Participants
The participants included in this analysis were a subset of RYGB surgery patients enrolled in a larger randomized controlled exercise trial (12) who completed the study intervention \( n = 119 \) and for whom we had complete and valid objectively measured PA data (PA inclusion criteria) and body composition measurements (dual-energy X-ray absorptiometry [DXA]). Ninety-six patients from two academic bariatric surgery practices (Pittsburgh, Pennsylvania, and Greenville, North Carolina) were included in this analysis (Figure 1). The study protocol was reviewed and approved by the human ethics committees of the University of Pittsburgh and East Carolina University, and all participants provided written informed consent. Male and female patients were eligible if they were between the ages of 21 and 60 years, had a BMI below 55 kg/m², underwent RYGB, and were not diabetic. All other inclusion/exclusion criteria are described elsewhere (12).

Study design
After an RYGB surgical procedure \( (76.7 \pm 24.7 \text{ d}) \), patients were randomized into one of two treatments for 6 months: an exercise training program (RYGB+EX) or lifestyle educational classes (RYGB). A detailed description of the intervention has been published elsewhere (12). Briefly, participants in the RYGB+EX group were required to participate in three to five exercise sessions per week of stationary cycling or walking, with at least one directly supervised session per week. Participants progressed so that a minimum of 120 min/wk of exercise was performed for the final 3 months of the program. A series of assessments was performed in each participant before and after the intervention. In this analysis, we included measurements of body composition by DXA and computed tomography (CT), accelerometry (PA and EE), and cardiorespiratory fitness \( (V_{O_{2}}_{\text{max}}) \). Identical procedures, equipment, and programs were utilized in both institutions as previously described (12).

Body composition
Weight and height were measured before surgery, before intervention, and after intervention, and BMI was calculated. FM and fat-free mass (FFM) were determined by DXA using a GE Lunar (GE Healthcare, UK).

Additionally, a single-slice CT protocol was carried out at L4-L5 and midthigh in order to assess total abdominal adipose tissue, visceral adipose tissue, abdominal subcutaneous adipose tissue, subfascial and intramuscular adipose tissue, deep abdominal adipose tissue, and thigh skeletal muscle mass (SMM). SliceOmatic image analysis software was used to quantify all tissues (Tomo Vision, Montreal, California).

RMR, energy intake, and cardiorespiratory fitness
RMR was measured by indirect calorimetry minutes with a ventilated canopy system cart (Parvo Medics, Sandy, Utah) following an overnight fast protocol as described previously (9). The last 15 minutes were used to calculate respiratory quotient \( (V_{C_{2}}/V_{O_{2}}) \) and EE.

Energy intake was estimated based on energy deficit between pre- and postintervention time periods as described in the literature (18). Energy equivalents for FM and FFM from DXA and TDEE from an armband device were utilized to calculate the energy deficit as follows:

\[
\text{Energy deficit} = \Delta FM \times 9.3 \text{kcal} \cdot \text{g}^{-1} \quad + \Delta \text{FFM} \times 1.1 \text{kcal} \cdot \text{g}^{-1}
\]

\[
\text{Energy intake} = \text{TDEE} + \text{Energy deficit}
\]

\( V_{O_{2}}_{\text{max}} \) was measured during a progressive exercise test on a cycle ergometer. A breath-by-breath system was used to measure \( V_{O_{2}} \) and \( V_{C_{2}} \) (MOXUS, AEI) (12).

TDPA and TDEE
TDPA (min/d) and TDEE (kcal/d) variables were measured with a triaxial accelerometer/temperature sensor (SenseWear Armband, Pittsburgh, Pennsylvania) that has been validated against doubly labeled water (16). Participants were instructed to wear the device on their right arm over a minimum of 7 days, within 3 weeks of the beginning of intervention and during the last week of intervention. Only data collected over 21 hours and 30 minutes per day (90% of day duration) and over 4 days were accepted for statistical analysis.
Exercise time was recorded by an exercise physiologist in charge of the intervention.

Our device provides metabolic equivalent of task (MET) values with a minute-by-minute resolution. International MET criteria cutoffs were used to obtain PA and EE dimensions: sedentary < 1.5 METs; light = 1.5 to ≤ 3.0 METs; moderate = 3.0 to ≤ 6.0 METs; vigorous = 6.0 to ≤ 9.0 METs (19). PA dimensions were quantified by adding all minutes pooled in each category, while EE was calculated by minute (EE [kcal/min] = [MET × weight(kg)]/60) for each PA category. Net EE variables were calculated in the same way by subtracting RMR (NetEE [kcal/min] = EE[kcal/min] − RMR[kcal/min]). Additionally, we calculated:

\[
\text{NEPA (Nonexercise Physical Activity) (min/d)} = \text{TDPA} - \text{Exercise time}
\]

Where TDPA was the sum of all minutes ≥ 1.5 METs; exercise time was recorded as the combined time from both direct supervision in our facilities and self-reported by the participants when performing structured exercise outside the centers.

\[
\text{Net PAEE} = \text{PAEE} - (\text{PA[min/d]} \times \text{RMR[kcal/min]})
\]

Where PAEE was the gross or absolute EE in all minutes ≥ 1.5 METs; PA was all minutes ≥ 1.5 METs; and RMR was resting metabolic rate.

\[
\text{NetSedEE} = \text{SedEE} - [(\text{RMR(kcal/min)} \times 0.90 \times \text{SleepTime(min/d)}) + (\text{RMR(kcal/min)} \times \text{Lying down(min/d)})] + (\text{RMR(kcal/min)} \times \text{SedTime(min/d)})
\]

Where SedEE was the gross or absolute EE in all minutes < 1.5 METs and SleepTime and Lying down were all minutes reported as sleeping and lying down provided by the accelerometer.
The variability in the change in PA in both intervention groups encouraged us to better understand the roles of both PA and EE. One approach we took was to analyze differences across quartiles of daily step quartile.

**Statistical analysis**

All variables were reported as means and standard deviations (SD). Differences between RYGB+EX and RYGB groups at preintervention time were analyzed by independent sample t test and proportions of sex and ethnicity by χ² analysis.

Repeated measures analysis (2×2 ANCOVA) was carried out to compare differences between RYGB+EX and RYGB after the intervention period. PreWeight (pre surgery), randomization time, and age were covariates for all comparisons; TDEE and RMR were additionally adjusted to their predicted values (Supporting Information Table S1). To examine associations specifically with structured exercise, body composition variables were also adjusted for moderate and vigorous physical activity (MVPA) in this analysis. Interactions between the group factor and covariates were also analyzed.

In order to analyze a dose-response association between TDPA (steps/day) and EE, PA, and body composition variables, quartiles of change in daily steps were calculated. Changes (Δ) in body composition, EE, and PA variables were used as dependent variables in a general linear model where the quartile group was the main factor, and comparisons were adjusted for PreWeight, age, and randomization time. TDEE and RMR were adjusted to their prediction equations (Supporting Information Table S1). When daily step quartiles variable was a significant predictor of any dependent variable, Tukey’s post hoc tests were carried out in order to detect differences between daily step quartile groups. Paired sample t tests of the single measurements (post–pre) were used to confirm differences before and after intervention in each quartile.
Finally, stepwise regression analyses were conducted to estimate whether EE (absolute and net variables) and PA variables could predict changes of weight and FM. Age, ethnicity, sex, PreWeight, VO_{2max}, and RMR were included as independent variables.

Significance was accepted at $P < 0.05$. Software JMP 12.0 was used for all treatments.

**Results**

Both EX+RYGB and RYGB groups had similar proportions of women/men (42/4 and 43/7, EX+RYGB and RYGB, respectively; $\chi^2 = 0.613$, $P = 0.434$), Caucasians/African Americans (37/8 and 42/8, EX+RYGB and RYGB, respectively; $\chi^2 = 0.053$, $P = 0.817$), and randomization times (75 $\pm$ 25 vs. 78 $\pm$ 25 d, $P < 0.05$). Respiratory quotient values above 1.00 and below 0.65 were removed from the analysis where RMR was included (RYGB = 7 and RYGB+EX = 2). On average, the patients wore PA monitors 7.11 $\pm$ 1.85 days for 23.32 $\pm$ 0.38 h/d pre intervention, which did not change after intervention (Supporting Information Table S1). Data for descriptive variables before surgery are presented in Table 1. Body composition, EE, and PA variables were similar between groups at the time of randomization in the trial, except for TDPA (min/d), light PA, and EE of daily light PA (LightEE) (Table 1). At the time that patients were randomized in the trial, participants had lost 14.1% ($-45.3$ to $-1.3$ kg) of their weight.

**Effects of the exercise intervention on body composition, EE, and PA**

After 6 months of intervention, both the RYGB + EX and RYGB groups had further reduced body weight, FM, and FFM ($-22.6 \pm 6.9$ vs. $-22.5 \pm 9.2$ kg, $-20.3 \pm 6.5$ vs. $-19.6 \pm 8.1$ kg, and $-1.43 \pm 2.6$ vs. $-1.1 \pm 2.5$ kg, respectively; within-subject time effect $P < 0.05$).

Both RYGB and RYGB+EX groups significantly increased their steps per day and their amount of time spent in light, moderate, vigorous, and TDPA, although these increases were not different between groups. Both groups decreased the amount of sedentary time and increased their levels of MVPA-related EE, but these increases were also not different between groups (Supporting Information Table S1). The magnitude of these increases in activity-related EE was not sufficient, however, to overcome the decrease in RMR (metabolic adaptation); thus, TDEE was similarly decreased in both groups. RYGB+EX increased NEPA to a significantly lesser extent than RYGB (+47.6 vs. +86.4 min/d, $P < 0.05$; Figure 2). Additionally, the proportion of patients who reduced NEPA was significantly higher in RYGB+EX than in RYGB (29.0% vs. 10.0%; $\chi^2 = 5.625$, $P < 0.05$). Exercise time for RYGB+EX was 160.9 $\pm$ 150.2 min/wk on average.

**Changes of body composition, PA, and EE across quartiles of change in daily steps**

The key objective of this analysis was to examine changes in body weight and body composition according to objectively measured PA irrespective of intervention assignment. Preintervention PA and EE variables are shown in Table 2. There were significant differences in all PA times and PAEE variables across steps per day quartiles ($P < 0.005$, Table 2). The highest quartile had a significantly greater increase in TDPA, MVPA, light PA, PAEE, LightEE, EE of daily MVPA, and reduction in sedentary time compared to the lowest quartile (Table 3). Conversely, daily steps and PA were significantly reduced, and sedentary time was not significantly reduced (within-subjects effect, Table 3) during intervention in the lowest quartile. Energy intake estimated by the intake-balance method (18) was not significantly different across quartiles (Table 2).

Those in the quartile representing highest change in steps per day lost significantly more body weight and body FM compared to the lowest quartile (Figure 3), and there was a trend toward greater weight and FM loss in the other higher quartiles. Regional adiposity measures from CT followed a similar pattern: change in total abdominal adipose tissue was significantly reduced more in the 4th compared to the 3rd quartile; similarly, a trend for a greater reduction in change in visceral adipose tissue and subfascial and intramuscular adipose tissue was observed (Figure 3). Regarding FFM and SMM, the 4th and 3rd quartiles (those with the highest levels of steps per day) lost less SMM than the 1st quartile ($-3.1 \pm 7.0$ and $-4.5 \pm 6.3$ cm$^2$ vs. $-30.2 \pm 7.0$ cm$^2$; $P < 0.05$).

![Figure 2](image-url)
### TABLE 2 Prerandomization characteristics of the participants by quartiles of change in daily steps across the 6-month intervention period

|                | Q1 (n = 24) | Q2 (n = 24) | Q3 (n = 24) | Q4 (n = 24) | Q5 (n = 24) |
|----------------|-------------|-------------|-------------|-------------|-------------|
|                | Mean SD     | Mean SD     | Mean SD     | Mean SD     | Mean SD     |
| **Age (y)**    | 39.50 ± 9.8 | 40.63 ± 10.6| 43.92 ± 7.5 | 39.38 ± 11.2|             |
| **Sex (F/M)**  | 22/2        | 22/2        | 19/5        | 22/2        |             |
| **PreWeight (kg)** | 115.9 ± 12.7| 122.6 ± 23.6| 125.2 ± 26.5| 134.7 ± 30.6|             |
| **BMIPre (kg/m²)** | 42.9 ± 4.4  | 43.7 ± 7.1  | 44.8 ± 7.0  | 48.2 ± 9.0  |             |
| **BMI (kg/m²)** | 36.4 ± 4.1  | 37.1 ± 5.8  | 38.8 ± 6.6  | 42.0 ± 8.2  | 1            |
| **RT (min/d)** | 82.0 ± 24.2 | 82.3 ± 26.2 | 78.4 ± 19.3 | 65.1 ± 25.6 | 1            |
| **Weight (kg)** | 98.7 ± 13.9 | 103.7 ± 17.9| 108.4 ± 24.9| 117.5 ± 28.0| 1            |
| **BMI (kg/m²)** | 46.0 ± 8.9  | 48.6 ± 11.4 | 51.1 ± 15.8 | 57.9 ± 17.2 | 1            |
| **FFM (kg)**   | 51.0 ± 8.1  | 52.4 ± 8.9  | 53.7 ± 10.8 | 52.3 ± 7.7  |             |
| **WearT (h/d)**| 23.3 ± 0.2  | 23.1 ± 1.2  | 23.3 ± 0.4  | 23.3 ± 0.5  |             |
| **Steps (steps/d)** | 7884.6 ± 2536.3| 6533.6 ± 3024.8| 5175.2 ± 1717.7| 4343.2 ± 1885.2| 1,2         |
| **Sed (min/d)** | 650.1 ± 106.0| 692.2 ± 122.2| 705.0 ± 119.3| 740.0 ± 135.9| 1            |
| **MVPA (min/d)**| 56.5 ± 25.9 | 47.2 ± 36.1 | 32.5 ± 27.9 | 28.0 ± 23.9 | 1            |

Suffix ‘Pre’ refers to variables measured pre surgery. 1, 2, 3, and 4 indicate significant differences with first, second, third, and fourth quartile (P < 0.05). RT, randomization time; FM, fat mass; FFM, fat-free mass; WearT, wear time; Sed, sedentary time without lying down and sleeping time; MVPA, moderate and vigorous physical activity time.

### TABLE 3 Changes in body composition, physical activity, and energy expenditure variables across quartiles of change in daily steps after intervention

|                | Q1 (n = 24) | Q2 (n = 24) | Q3 (n = 24) | Q4 (n = 24) | Q5 (n = 24) |
|----------------|-------------|-------------|-------------|-------------|-------------|
|                | Mean SD     | Mean SD     | Mean SD     | Mean SD     | Mean SD     |
| **Steps (steps/d)** | -1,419 ± 1,148 | 2,3,4,* | 406 ± 351 | 1,3,4,* | 1,618 ± 332 | 1,2,4,* | 3,446 ± 1,833 | 1,2,3,* |
| **Group (RYGB+EX/RYGB)** | 14/10 | 10/14 | 10/14 | 12/12 |             |
| **TDPA (min/d)** | 19.64 ± 66.22 | 34 | 54.08 ± 55.60 | 4* | 82.96 ± 49.95 | 1,4* | 131.86 ± 89.48 | 1,2,3* |
| **MVPAs (min/d)** | 11.76 ± 73.46 | 4 | 39.70 ± 59.91 | 4* | 72.32 ± 52.92 | 4* | 144.61 ± 130.0 | 1,2,* |
| **LightPAs (min/d)** | 26.76 ± 66.04 | 4* | 36.54 ± 45.26 | 4* | 63.61 ± 49.23 | 4* | 84.41 ± 62.76 | 1,2,* |
| **Sed (min/d)** | -10.04 ± 107.3 | 4 | -51.17 ± 55.85 | 4* | -82.00 ± 53.81 | 4* | -125.23 ± 93.51 | 1,2,* |
| **TDEEs (kcal/d)** | -461.60 ± 52.49 | 34,* | -337.38 ± 51.97 | * | -233.05 ± 359.1 | 1,* | -205.07 ± 56.04 | 1* |
| **PAEs (kcal/d)** | -156.7 ± 50.37 | 34,* | 9.98 ± 48.08 | 4 | 133.5 ± 49.2 | 1,4* | 361.9 ± 51.51 | 1,2,3* |
| **LightEEs (kcal/d)** | -63.10 ± 31.79 | 34,* | -26.18 ± 30.35 | 4 | 69.50 ± 31.08 | 1* | 123.87 ± 32.51 | 1,2,* |
| **MVEEs (kcal/d)** | -93.56 ± 30.82 | 23,4* | 36.17 ± 29.42 | 1,4 | 64.05 ± 30.13 | 1,4* | 238.02 ± 31.52 | 1,2,3* |
| **RMRs (kcal/d)** | -20.34 ± 59.06 | 4 | -52.73 ± 58.57 | 4 | -119.42 ± 54.73 | 4* | -124.68 ± 61.8 | 1,* |
| **PALs (kcal/d)** | -0.249 ± 0.248 | 34,* | -0.169 ± 0.268 | * | -0.025 ± 0.266 | 4 | -0.027 ± 0.416 | 1 |

1, 2, 3, and 4 indicate significant differences with the first, second, third, and fourth quartile (P < 0.05). A main effect was found in all groups where multiple comparisons were performed.

* Differences adjusted to randomization time, preintervention weight/fat mass (FM), and age.

**TDEE changes adjusted to estimated TDEE from a specific equation with preintervention data (TDEE = 199.71 + 44.588 × FFM (kg) + 152.46 × [F = 1, M = 0]).**

**RMR changes adjusted to estimated RMR from a specific equation with preintervention data (RMR = 2.24 × FFM + 26.77 × FFM – 5.45 × Age – 174 × Race + 449) and randomization period.**

*Indicates a significant change between pre- and postintervention periods for that individual quartile (P < 0.05).

TDPA, total daily physical activity; NEPA, nonexercise physical activity (NEPA = TDPA – (min/wk of exercise)/7); MVPA, moderate and vigorous physical activity; PAEE, total daily physical activity energy expenditure; RMR, resting metabolic rate; Light, daily energy expenditure of daily physical activity; TDEE, total daily energy expenditure; PAL, physical activity level (TDEE/RMR); MVEE, daily moderate to vigorous energy expenditure.
EE and PA predictors of weight and FM loss
The increase in daily steps and TDPA were associated with greater weight loss during the intervention (Figure 4). The strongest associations between weight loss and EE or PA variables, however, were with the decrease in sedentary time (ΔSedEE), even after adjusting for RMR (ΔNetSedEE). Early weight loss occurring after surgery and before the intervention trial was only modestly related to the amount of TDPA (r = −0.248, P = 0.0152) and steps (r = −0.213, P = 0.0380) that patients were performing prior to starting the trial. Nevertheless, after adjusting for early weight loss, the change in PA and sedentary time performed during the trial was still associated with weight loss (ΔTDPA r = −0.262; Δsteps r = −0.300; ΔSedT r = 0.256; ΔSedEE r = 0.803; ΔNetSedEE r = 0.628; P < 0.05).

In Figure 5, we present the models that best explain change in body weight and FM. Absolute EE variables (Table 4), ΔSedEE and ΔLightEE, and age explained 73.8% of weight loss and 70.6% of FM loss. When RMR was included in the prediction models, NetEE and RMR both contributed to the variance in weight and FM loss (Table 4). Beta coefficients indicated that greater reductions in SedEE, LightEE, and RMR were associated with greater weight and FM loss. These data indicate that both resting and activity-related EE were significantly associated with weight loss (Table 4).

The regression models including PA variables had lower coefficients of determination than those derived from EE. Light PA was a significant predictor of Δweight or ΔFM, and older patients lost less weight and FM (Table 4). The only significant predictor of less FFM loss was an increase in VO2max, which explained 8.8% of ΔFFM.

Discussion
Bariatric surgery can result in robust and sustained weight loss, although the variability in responses is increasingly being recognized as a problem for many patients. A decreased EE in response to weight loss, a so-called hypometabolism or metabolic adaptation, has been commonly proposed as a reason for variation in weight loss and weight regain. To date, there have been few investigations of PA or EE to explain variation in weight loss following RYGB surgery-induced weight loss. The main finding of this study was that...
PA and EE explained a significant amount of the variation in weight and body fat loss following RYGB surgery.

Effects of exercise on weight loss, body composition, and EE following surgery
Changes in nearly all parameters of daily EE, light to moderate PA, and sedentary time were similar in patients randomized to RYGB+EX and RYGB groups, despite the RYGB+EX group performing 160.9 min/wk of intentional exercise. There was a wide range, however, in reported exercise, and not all exercise sessions were supervised. Moreover, subjects in both diet (9) and bariatric surgery weight loss programs often increase their PA outside the confines of a structured exercise session or PA counseling (9,20). Ours is the first study to assess whether an exercise program might affect other components of PA in patients post bariatric surgery, which has limited other investigations lacking objective measurements of PA and EE (21-23) and which could confound the effects of exercise training. Although the exercise program participants did not reduce NEPA, their average increase in NEPA was significantly less than those not assigned to the exercise group. This finding is supported by recent evidence suggesting that structured exercise may affect NEPA (13,24), mainly in women (13). Estimated energy intake in our study, however, was not significantly different between groups (2,376 vs. 2,328 kcal/d, $P > 0.05$), which is not in accord with other studies suggesting confounding effects of exercise on

Figure 4 Simple correlations between change in weight and measures of physical activity (PA) and energy expenditure as measured by a device that combines a three-axis accelerometer and temperature sensors (SenseWear Armband). TDEE, total daily energy expenditure; SedEE, energy expenditure during sedentary time; NetTDEE = TDEE – resting metabolic rate (RMR); NetSedEE = SedEE – RMR; TDPA, total daily PA including light, moderate, and vigorous dimensions; STEPs, number of steps per day.
energy intake (25,26). Taken together, our data suggest that the similar weight and FM loss between RYGB and RYGB+EX could have been partially explained by NEPA as suggested in previous studies with (27) and without diet (28,29).

The modest increases in activity-related EE in patients performing structured exercise did not significantly compensate for the decrease in either resting EE or TDEE. These results are supported by our previous reports that moderate PA superimposed on a diet-induced weight loss program in subjects with severe obesity increases TDEE only in those subjects who perform more than 47 min/d (9). TDEE has also been reported to be significantly reduced after bariatric surgery, despite concomitant exercise (30,31), which supports our results. This reduction in EE could be associated with the weight loss and reduction in FFM as suggested in a recent review (3). FFM was only reduced by 1.35 kg during our intervention, so it seems unlikely that a decrease in FFM was the only mechanism responsible for the TDEE reduction. The decrease in RMR due to weight loss, either with or without the exercise, is consistent with a large body of literature (4,8,32,33), which could explain some of the decrease in TDEE, as RMR is a main component of TDEE. Both intervention groups had similar reductions in sedentary time, and changes in sedentary behavior did not seem to confound the intervention effects on PA or estimated EE, as reported in a recent study (20).

**Figure 5** Scatterplots between measured and predicted changes in weight (white dots) or fat mass (FM, black dots). Predicted values were estimated from regression models from (A) absolute changes in energy expenditure (EE) variables, (B) changes in NetEE variables, and (C) changes in physical activity (PA) dimensions.
Changes in PA
In this analysis, all PA and EE variables were changed across the groups (between-subjects effect), in accordance with a previous study, which utilized a similar analysis in a lifestyle intervention with participants with Class III obesity (9). The greater weight and body fat loss in those who performed more PA suggests that a change in PA is necessary in order to obtain significant changes. After adjusting for PreWeight and age, patients who increased by an average of 3,446 steps per day lost 6 kg more weight than patients who did not increase their steps per day. The quartile analysis also revealed larger reductions in regional adiposity, which extends results from our previous study reporting a dose-response association between minutes of exercise and abdominal adiposity (34) and steps per day and cardiometabolic risk factors (35). The loss of SMM measured by CT was attenuated in the highest quartile of steps per day, although FFM change was not different across quartiles. Further studies are needed to determine whether or not these changes associated with PA will also be associated with longer-term benefits in cardiometabolic risk or durability of weight loss and prevention of weight regain.

TABLE 4 Regression models for estimating change in body weight and fat mass from energy expenditure/net energy expenditure variables/physical activity variables, ethnicity, sex, and age

| Models from EE variables | Variable (Δ BW) | β   | SE  | R²   | t ratio | P     |
|-------------------------|-----------------|-----|-----|------|--------|-------|
| Intercept               | −18.636         | 2.549 | 7.31 | 0.116 | <0.001 |       |
| Age (y)                 | 0.205           | 0.053 | 0.061 | 2.2   | <0.001 |       |
| ∆SedEE (kcal/d)         | 0.021           | 0.005 | 0.635 | 4.38  | <0.001 |       |
| ∆LightEE (kcal/d)       | 0.020           | 0.005 | 0.042 | 4.02  | <0.001 |       |
| R² = 0.738              | RMSE (kg)       | 4.69 |
| Models from NetEE variables | Variable (Δ BW) | β   | SE  | R²   | t ratio | P     |
| Intercept               | −12.980         | 1.109 | 11.70 | <0.001 |       |
| ∆NetSedEE (kcal/d)      | 0.0325          | 0.003 | 0.435 | 10.86 | <0.001 |       |
| ∆RMR (kcal/d)           | 0.0198          | 0.003 | 0.173 | 6.01  | <0.001 |       |
| R² = 0.608              | RMSE (kg)       | 5.34 |
| Variable (Δ FM)         | β   | SE  | R²   | t ratio | P     |
| Intercept               | −15.120         | 2.291 | 6.77  | <0.001 |       |
| ∆SedEE (kcal/d)         | 0.028           | 0.002 | 0.570 | 12.62 | <0.001 |       |
| ∆LightEE (kcal/d)       | 0.014           | 0.003 | 0.094 | 4.68  | <0.001 |       |
| Age (y)                 | 0.159           | 0.047 | 0.040 | 3.38  | <0.01  |       |
| R² = 0.706              | RMSE (kg)       | 4.15 |

| Variable (Δ FM)         | β   | SE  | R²   | t ratio | P     |
|-------------------------|-----|-----|------|--------|-------|
| Intercept               | 10.91 | 0.978 | 11.16 | <0.0001 |       |
| ∆NetSedEE (kcal/d)      | 0.0297 | 0.003 | 0.416 | 11.25  | <0.0001 |       |
| ∆RMR (kcal/d)           | 0.0191 | 0.003 | 0.203 | 6.60   | <0.0001 |       |
| R² = 0.619              | RMSE (kg)       | 4.71 |

TABLE 4 (continued).

| Models from PA variables | Variable (Δ BW) | β   | SE  | R²   | t ratio | P     |
|-------------------------|-----------------|-----|-----|------|--------|-------|
| Intercept               | −12.78          | 5.497 | 2.33  | <0.022 |       |
| PreWeight (kg)          | −0.192          | 0.029 | 0.322 | <6.72  | <0.0001 |
| RandoTime (d)           | −0.088          | 0.031 | 0.080 | 2.84   | <0.01  |       |
| Age (y)                 | 0.221           | 0.076 | 0.044 | 2.92   | <0.01  |       |
| ∆Light (min/d)          | −0.034          | 0.012 | 0.047 | 2.76   | <0.01  |       |
| R² = 0.493              | RMSE (kg)       | 6.57 |

| Variable (Δ FM)         | β   | SE  | R²   | t ratio | P     |
|-------------------------|-----|-----|------|--------|-------|
| Intercept               | −12.02 | 5.117 | 2.35  | <0.05  |       |
| PreWeight (kg)          | −0.159 | 0.028 | 0.263 | <5.63  | <0.0001 |
| RandoTime (d)           | −0.078 | 0.030 | 0.086 | 2.80   | <0.01  |       |
| Age (y)                 | 0.179           | 0.068 | 0.042 | 2.63   | <0.01  |       |
| ∆Light (min/d)          | −0.023          | 0.011 | 0.033 | 2.15   | <0.05  |       |
| R² = 0.424              | RMSE (kg)       | 5.84 |

Table indicates difference between variables (post–preintervention period).

All variables were significant predictors of Δweight or ΔFM after stepwise regression analyses. The variables included in the analysis but without predictive significance were: (a) the models derived from EE variables (MAVEE, difference in EE of daily moderate and vigorous PA), energy intake, ARMR difference in PA level (TDEE/RMR), body weight before surgery, randomization time, sex, and ethnicity; (b) the models derived from NetEE variables (ΔLightEE, ∆MAVEE, energy intake, ∆PA level [TDEE/RMR], body weight before surgery, randomization time, sex, and ethnicity); (c) the models derived from PA variables (AMVPA [difference in daily moderate and vigorous PA], ΔSed, energy intake, ARMR, steps per day, sex, and ethnicity).

BW, body weight; EE, daily energy expenditure; FM, fat mass; Light, light physical activity; LightEE, energy expenditure of daily light physical activity; Net, all energy expenditure variables recalculated without proportional resting metabolic rate; PA, physical activity; RandoTime, randomization time; RMR, resting metabolic rate; Sed, awakened sedentary time; SedEE, energy expenditure of daily sedentary time; TDEE, total daily energy expenditure; RMR, root mean square error.

Prediction of weight loss and body composition
Various components of EE dimensions significantly correlated with FM and weight loss, which confirms findings from previous studies showing the predictive importance of RMR (36) or TDEE (3). LightEE was a significant predictor of weight and FM loss, which suggests that even light PA may play a role during the early phase of weight loss in these patients. The strong associations with sedentary time and SedEE support previous studies reporting sedentary behavior as an independent risk factor for health (37-39), even after accounting for the influence of RMR reduction. Finally, the model including the PA variables revealed that light PA was a significant predictor of weight and FM loss, which is supported by our quartile dose-response analysis. These results are in agreement with those from a previous study with energy restriction in which TDPA explained 7% of weight loss after 12 weeks of diet (40).

Our study of free-living subjects was limited to estimates rather than direct measures of TDEE or energy intake. However, we performed an internal validation of estimated TDEE with the SenseWear Armband with doubly labeled water in our laboratory and found a strong correlation in people with severe obesity (R = 0.83, TDEE by armband [2,980 ± 606 kcal/d] and doubly labeled water [3,036 ± 555 kcal/d]). Future studies should determine whether exercise or PA affects energy intake following bariatric surgery. Additional studies
should also investigate specific levels of PA that may be required to produce a longer-term negative energy balance to overcome the metabolic adaptation observed with energy restriction. In addition, it will be important to determine the longer-term effects of increased PA on cardiometabolic risk independently of weight loss following bariatric surgery. Finally, the generalization of our results must be limited by the inclusion and exclusion criteria.

Conclusion

In summary, RYGB nondiabetic patients who perform modest amounts of PA and decrease sedentary time following RYGB lose more weight and FM while maintaining higher lean body mass. While structured exercise specifically increases cardiorespiratory fitness and promotes greater improvements in insulin sensitivity independent of surgery-induced weight loss (12,34), NEPA and EE are also important contributors to weight loss and body composition changes following RYGB surgery and should be promoted to enhance weight loss. Future studies are needed to better understand the roles of longer-term exercise, PA, and EE in bariatric surgery patients as likely mediators of weight loss and weight loss maintenance.

Acknowledgments

Thanks to Nicole L. Helbling, Marisa E. Desimone, Frederico Tol- edo, and Maja Stefanovic for clinical support, Steve Anthony for intervention, indirect calorimetry, and DXA, Alex Desimpes for CT analysis, and the staff at the Clinical Translational Research Center, University of Pittsburgh.

© 2017 The Obesity Society

References

1. Pories WJ. Bariatric surgery: risks and rewards. J Clin Endocrinol Metab 2008;93: S89-S96.
2. de Hollanda A, Ruiz T, Jimenez A, Flores L, Lacy A, Vidal J. Patterns of weight loss response following gastric bypass and sleeve gastrectomy. Obes Surg 2015;25:1177-1183.
3. Thivel D, Brakoniecki K, Duche P, Morio B, Boirie Y, Laferrere B. Surgical weight loss: impact on energy expenditure. Obes Surg 2013;23:255-266.
4. Browning MG, Franco RL, Cyrus JC, Celi F, Evans RK. Changes in resting energy expenditure in relation to body weight and composition following gastric restriction: a systematic review. Obes Surg 2016;26:1607-1615.
5. Hall KD, Heymsfield SB, Kemnitz JW, Klein S, Schoeller DA, Speakman JR. Energy balance and its components: implications for body weight regulation. Am J Clin Nutr 2012;95:989-994.
6. Dullao AG, Jacquet J, Montani JP, Schutz Y. Adaptive thermogenesis in human body weight regulation: more of a concept than a measurable entity? Obes Rev 2012;13 (Suppl 2):105-121.
7. Camps SG, Verhoef SP, Westerterp KR. Weight loss, weight maintenance, and adaptative thermogenesis. Am J Clin Nutr 2013;97:990-994.
8. Speakman JR, Selman C. Physical activity and resting metabolic rate. Proc Nutr Soc 2003;62:621-634.
9. DeLany JP, Kelley DE, Hames KC, Jakicic JM, Goodpaster BH. Effect of physical activity on weight loss, energy expenditure, and energy intake during diet induced weight loss. Obesity (Silver Spring) 2014;22:363-370.
10. Livhits M, Mercado C, Yermilov I, et al. Behavioral factors associated with successful weight loss after gastric bypass. Am Surg 2010;76:1139-1142.
11. Marches F, De Sario O, Reggiani V, et al. Road running after gastric bypass for morbid obesity: rationale and results of a new protocol. Obes Surg 2015;25:1162-1170.
12. Coen PM, Tanner CJ, Helbling NL, et al. Clinical trial demonstrates exercise following bariatric surgery improves insulin sensitivity. J Clin Invest 2015;125:248-257.
13. Fedewa MV, Hathaway ED, Williams TD, Schmidt MD. Effect of exercise training on non-exercise physical activity: a systematic review and meta-analysis of randomized controlled trials. Sports Med 2017;47:1171-1182.

Obesity | VOLUME 25 | NUMBER 7 | JULY 2017

14. King WC, Chen JY, Bond DS, et al. Objective assessment of changes in physical activity and sedentary behavior: pre- through 3 years post-bariatric surgery. Obesity (Silver Spring) 2015;23:1143-1150.
15. Reece JD, Barry V, Fuller DK, Caputo J. Validation of the SenseWear Armband as a measure of sedentary behavior and light activity. J Phys Act Health 2015;12:122-137.
16. Mackey DC, Manini TM, Schoeller DA, et al. Validation of an armband to measure daily energy expenditure in older adults. J Gerontol A Biol Sci Med Sci 2011;66:1108-1113.
17. Coen PM, Goodpaster BH. A role for exercise after bariatric surgery? Diabetes Obes Metab 2016;18:16-23.
18. de Jonge L, DeLany JP, Nguyen T, et al. Validation study of energy expenditure and intake during calorie restriction using doubly labeled water and changes in body composition. Am J Clin Nutr 2007;85:73-79.
19. Thompson D, Batterham AM. Towards integrated physical activity profiling. PLoS One 2013;8:e56427. doi:10.1371/journal.pone.0056427
20. Creet DB, Schuh LM, Reed CA, et al. A randomized trial comparing two interventions to increase physical activity among patients undergoing bariatric surgery. Obesity (Silver Spring) 2016;24:1660-1668.
21. Lévy-Marcos M, Mercado C, Yermilov I, et al. Exercise following bariatric surgery: systematic review. Obes Surg 2010;20:657-665.
22. Bond DS, Jakicic MJ, Unick JL, et al. Pre- to postoperative physical activity changes in bariatric surgery patients: self report vs. objective measures. Obesity (Silver Spring) 2010;18:2395-2397.
23. Panosian J, Ding SA, Wewalka M, et al. Physical activity in obese type 2 diabetes after gastric bypass or medical management. Am J Med 2017;130:83-92.
24. Melanson EL, Keadle SK, Donnelly JE, Braun B, King NA. Resistance to exercise-induced weight loss: compensatory behavioral adaptations. Med Sci Sports Exerc 2013;45:1600-1609.
25. McLaughlin R, Malkova D, Nimmo MA. Spontaneous activity responses to exercise in males and females. Eur J Appl Physiol 2006;90:1055-1061.
26. Stubbs RJ, Hughes DA, Johnstone AM, et al. Rate and extent of compensatory changes in energy intake and expenditure in response to altered exercise and diet composition in humans. Am J Physiol Regul Integr Comp Physiol 2004;286:R350-R358.
27. Kempen KP, Saris WH, Westerterp KR. Energy balance during an 8-wk energy-restricted diet with and without exercise in obese women. Am J Clin Nutr 1995;62:722-729.
28. Herrmann SD, Willis EA, Honas JJ, Lee J, Washburn RA, Donnelly JE. Energy intake, nonexercise physical activity, and weight loss in responders and nonresponders: the Midwest Exercise Trial 2. Obesity (Silver Spring) 2015;23:1539-1549.
29. Rosenkilde M, Auerbach P, Reichkendler MH, Ploug T, Stallknecht BM, Sjodin A. Body fat loss and compensatory mechanisms in response to different doses of aerobic exercise—a randomized controlled trial in overweight sedentary males. Am J Physiol Regul Integr Comp Physiol 2012;303:R571-R579.
30. Das SK, Roberts SB, Kehayias JJ, et al. Body composition assessment in extreme obesity and after massive weight loss induced by gastric bypass surgery. Am J Physiol Regul Integr Comp Physiol 2012;297:R340-R346.
31. van Gemert WG, Westerterp KR, van Acker BA, et al. Energy, substrate and protein metabolism in morbid obesity before, during and after massive weight loss. Int J Obes Relat Metab Disord 2000;24:711-718.
32. Johanssen DL, Knuth ND, Huizenga R, Rood JC, Ravussin E, Hall KD. Metabolic slowing with massive weight loss despite preservation of fat-free mass. J Clin Endocrinol Metab 2012;97:2304-2309.
33. Schwartz A, Doucet E. Relative changes in resting energy expenditure during weight loss: a systematic review. Obes Rev 2010;11:531-547.
34. Woodfield TL, Carnero EA, Standley RA, et al. Dose response of exercise training following Roux-en-Y gastric bypass surgery: a randomized trial. Obesity (Silver Spring) 2015;23:2454-2461.
35. Weferf JF, Woodfield TL, Carnero EA, et al. Relationship among physical activity, sedentary behaviors, and cardiometabolic risk factors during gastric bypass surgery-induced weight loss. Surg Obes Relat Dis 2017;13:210-219.
36. Ott MT, Ott L, Haack D, Colacchio TA, Lewis J. The MEE/PEE ratio as a predictor of excess weight loss for up to 1 year after vertical banded gastroplasty. Arch Surg 1992;127:1089-1093.
37. Thompson D, Peacock O, Western M, Batterham AM. Multidimensional physical activity: an opportunity, not a problem. Exerc Sport Sci Rev 2015;43:67-74.
38. Yates T, Henson J, Edwardson CL, et al. Objective measured sedentary time and associations with insulin sensitivity: importance of reallocating sedentary time to physical activity. Prev Med 2015;76:79-83.
39. inman TB, Knabel D, Strath SJ, et al. Associations of reducing sedentary time with vascular function and insulin sensitivity in older adults. Am J Hypertens 2016;29:46-53.
40. Bonomi AG, Soenen S, Goris AH, Westerterp KR. Weight-loss induced changes in physical activity and activity energy expenditure in overweight and obese subjects before and after energy restriction. PLoS One 2015;18:e59641. doi:10.1371/journal.pone.0059641.