Published in final edited form as:

Med Sci Sports Exerc. 2014 December ; 46(12): 2286–2294. doi:10.1249/MSS.0000000000000354.

Nonexercise Energy Expenditure and Physical Activity in the Midwest Exercise Trial 2

Erik A. Willis¹, Stephen D. Herrmann², Jeffery J. Honas¹, Jaehoon Lee³, Joseph E. Donnelly¹, and Richard A. Washburn¹

¹Cardiovascular Research Institute, Department of Internal Medicine, The University of Kansas Medical Center, Kansas City, KS

²Health, Physical Education & Recreation, Augustana College, Sioux Falls, SD

³Institute for Measurement, Methodology, Analysis, and Policy, Texas Tech University, Lubbock, TX

Abstract

PURPOSE—To examine compensatory changes in non-exercise energy expenditure (NEEx) and non-exercise physical activity (NEPA) in response to an aerobic exercise training program.

METHODS—Ninety-two overweight/obese (BMI 25–39.9 kg·m⁻²) sedentary young adults (18–30 years) completed a 10-month randomized clinical efficacy trial of aerobic exercise 5 d·wk⁻¹ at either 400 kcal·session⁻¹ ($n=37$), 600 kcal·session⁻¹ ($n=37$) or control ($n=18$). Total daily energy expenditure (TDEE) and resting metabolic rate (RMR) were measured at months 0 and 10. NEPA was measured by accelerometer at months 0, 3.5, 7, and 10. NEEx was calculated by [(TDEE*0.9)–RMR]–net EEEx (EEEx–RMR). Mixed modeling was used to examine differences between groups (group effect), within groups (time effect) and group-by-time interaction for NEEx and NEPA.

RESULTS—Within the exercise groups, there were no significant effects (all $p>0.05$) of group, time, or group-by-time interaction for NEPA. Additionally, there were no significant within or between group differences for change in NEEx. However, activity cts·min⁻¹ were significantly higher ($p<0.001$) in the 600 kcal·session⁻¹ group (346 ± 141 min·d⁻¹) vs. controls (290 ± 106 min·d⁻¹) at month 7 and significantly higher ($p<0.001$) in both the 600 kcal·session⁻¹ (345 ± 163 min·d⁻¹) and 400 kcal·session⁻¹ groups (317 ± 146 min·d⁻¹) vs. controls (277 ± 116 min·d⁻¹) at 10 months.

CONCLUSION—A 10-month aerobic exercise training program in previously sedentary, overweight and obese young adults was not associated with compensatory decreases in NEEx or NEPA. Results suggest that overweight and obese individuals do not become less physically active or spend more time in sedentary pursuits in response to exercise.

Corresponding Author: Erik Willis, Energy Balance Laboratory, 1301 Sunnyside Ave., Room 100, Lawrence, KS 66045, (785) 864-0776, ewillis@ku.edu.

Conflict of Interest

The authors report no conflict of interest

Keywords

Compensation; Exercise; Doubly-Labeled Water; Accelerometer; Obesity

INTRODUCTION

Exercise is recommended for weight management by several governmental agencies and professional organizations (1, 6). Compared with weight loss induced by energy restriction, weight loss achieved by exercise is composed predominantly of fat mass, while fat-free mass is preserved (7) and resting metabolic rate (RMR) is generally unchanged (30) or slightly increased (27). These factors may be associated with improved long term weight loss maintenance. However, several reports have demonstrated that the accumulated negative energy balance induced by an exercise intervention alone is less than theoretically predicted for the imposed level of exercise-induced energy expenditure (3, 18) most likely due to compensatory changes in energy intake, non-exercise energy expenditure (NEEx), or both. These compensatory changes could reduce the magnitude of exercise induced weight loss. Compensatory changes in energy intake and/or NEEx are also suggested by studies reporting no additional weight loss with increased exercise dose (3, 8, 29).

As early as 1980, Epstein and Wing (11) suggested that a reduction on NEEx might compensate for prescribed exercise training, thus resulting in little to no change in total daily energy expenditure and no, or minimal, exercise induced weight loss. A number of short term (2 to 14 days) (2, 19–21, 31, 32, 36, 40), non-randomized (4, 5, 13, 17, 22–24, 26) and randomized trials (3, 12, 16, 28, 29, 35) have evaluated the effect of exercise training on NEEx or non-exercise physical activity (NEPA) with mixed results. Irrespective of study design (i.e., short-term cross-over, non-randomized, randomized trials) the majority of studies do not observe reductions in reported NEPA (3, 19, 20, 29, 36) or NEEx (5, 12, 16, 17, 21, 24, 28, 31, 32, 35, 40) in response to prescribed aerobic exercise. Studies that reported decreased NEEx (4, 13, 26) or NEPA (22, 23) in response to prescribed exercise utilized non-randomized designs and were generally conducted in small samples (15/group) of overweight or obese older adults (i.e., >55 years). Assessments of change in NEEx rather than NEPA in response to prescribed aerobic exercise are particularly relevant in the context of weight management. However, no trials have assessed NEEx using state-of-the-art measures of total daily energy expenditure (doubly labeled water) resting metabolic rate (indirect calorimetry) and exercise energy expenditure (EEEx) (indirect calorimetry) (37). Data from the Midwest Exercise Trial-2 (MET-2) afforded an opportunity to examine the effect of prescribed aerobic exercise on both NEEx (doubly labeled water with both RMR and EEEx assessed by indirect calorimetry) and NEPA (accelerometer) in a sample of previously sedentary, overweight/obese young adult men and women. Briefly, MET-2 randomized overweight or obese individuals (BMI 25–40 kg·m⁻²), age 18–30 years to a 10 month, 5 d·wk⁻¹ supervised exercise intervention at 2 levels of exercise energy expenditure (400 or 600 kcal·session⁻¹) or non-exercise control. The primary aims of MET-2 were to evaluate the role of aerobic exercise without energy restriction on weight and body composition; however, several secondary outcomes, including changes in resting metabolic rate, NEPA and NEEx, and energy intake were included *a-priori* in the original study

design. MET-2 was powered to detect between group differences in weight change over time and to determine if weight change was equivalent in men and women. NEPA and NEEEx were unpowered secondary outcomes. A detailed description of the design and methods for MET-2 (9), and the results for the primary aims (8) have been published previously. Data regarding changes in energy and macronutrient intake and the effect of changes in NEPA and NEEEx on weight change will be reported separately.

METHODS

Participants

Participants were men and women (age 18–39 years, BMI 25–40 kg·m⁻²) who were able to exercise and willing to be randomized into 1 of the 3 study groups. Potential participants were excluded for the following reasons: A history of chronic disease (i.e., diabetes, heart disease, etc.), elevated blood pressure (>140/90), lipids (cholesterol >6.72 mmol·L⁻¹; triglycerides >5.65 mmol·L⁻¹), or fasting glucose (>7.8 mmol·L⁻¹), use of tobacco products, taking medications that would affect physical performance (i.e., beta blockers, metabolism, thyroid, or steroids), inability to perform laboratory tests or participate in moderate-to-vigorous intensity exercise, and planned physical activity greater than 500 kcal·wk⁻¹ as assessed by recall (33). Participants provided written informed consent prior to engaging in any aspect of the trial and were compensated for participation. Approval for this study was obtained from the Human Subjects Committee at the University of Kansas-Lawrence.

Randomization and blinding

Participants were stratified by sex and randomized by the study statistician (~80% exercise; ~20% control). All participants were instructed to continue their typical patterns dietary intake over the duration of the 10 month intervention. The blinding of participants to group assignment was not possible due to the nature of the intervention. However, both investigators and research staff were blinded at the level of outcome assessments, data entry and data analysis.

Exercise Training

Participants completed 5 d·wk⁻¹ of supervised exercise consisting primarily of walking and jogging. Alternate activities (e.g., elliptical, bicycle) were allowed for 20% of the exercise sessions. Exercise intensity was initially set at 70% heart rate max (HR) and slowly progressed to 80% HR max by month five. Exercise progressed from 150 kcal·session⁻¹ at intervention onset to the target EEEx (400 or 600 kcal·session⁻¹) at the end of month 4 and remained at target for the final 6 months of the study. Exercise was supervised by trained research staff and the duration and intensity of all exercise sessions were verified by a HR monitor (RS 400; Polar Electro Inc., Woodbury, NY). A valid exercise session was defined as ± 4 beats·min⁻¹ of target HR for a duration sufficient to achieve the target EEEx (400 or 600 kcal·session⁻¹). The average duration of an exercise session after reaching the target EEEx was 39 ± 10 min in the 400 kcal·session⁻¹ group and 55 ± 12 min in the 600 kcal·session⁻¹ group. Due to the efficacy design, completion of 90% of exercise sessions was an *a-priori* definition of per protocol, thus our analysis included only participants meeting this criteria.

The duration of exercise required to elicit the targeted EEEx (either 400 or 600 kcal-session⁻¹) was determined individually for each participant. At the baseline assessment, treadmill speed was set at 3 mph with a 0% grade and was adjusted by increments of 0.5 mph and 1% grade until the participant reached 70% HR max. Maximal HR was the highest HR rate achieved during the assessment of maximal aerobic capacity (9). EEEx was then assessed over a 15 minute interval (1-minute epochs) using a ParvoMedics TrueOne2400 indirect calorimetry system (ParvoMedics Inc., Sandy, UT). The average EEEx (kcal·min⁻¹) over the 15 minute interval was calculated from measured oxygen consumption and carbon dioxide production using the Weir equation (38). This value was used to provide the goal for the duration of exercise sessions for the first month of the intervention. For example: prescribed EEEx during month 1 = 150 kcal-session⁻¹, EEEx = 9.2 kcal·min⁻¹, exercise duration = 150 kcal-session⁻¹ divided by 9.2 kcal·min⁻¹ = 16 minutes-session⁻¹. Similar procedures to determine exercise duration, at either 70% or 80% HR max, were conducted at the end of each month over the course of the 10 month intervention to adjust for potential effects of changes in both body weight and cardiovascular fitness on EEEx. All exercise sessions and assessments of EEEx were preceded by a brief warm up on the treadmill (~2 minutes, 3–4 mph, 0% grade). Treadmill speed and grade were subsequently increased to achieve the prescribed target HR.

Control group—Participants assigned to the non-exercise control group were instructed to continue their typical patterns for physical activity and dietary intake over the duration of the 10 month study. With the exception of assessment of EEEx, the same outcome assessments were completed with both the exercise and control groups.

Outcomes

All assessments were completed by trained research assistants.

Resting Metabolic Rate (RMR)—RMR was assessed at baseline and 10 months by open circuit indirect calorimetry. Participants reported to our laboratory between 6 and 10 a.m. after a 12 hour fast and 48 hour abstention from aerobic exercise (14) and rested quietly for 15 minutes in a temperature controlled (21–24°C) isolated room. Subsequently, participants were placed in a ventilated hood for assessment of VO₂ and VCO₂ for a minimum of 35 minutes using a ParvoMedics TrueOne 2400 indirect calorimetry system (ParvoMedics Inc., Sandy, UT). Criteria for a valid RMR was a minimum of 30 minutes of measure values with <10% average standard deviation across the last 30 minutes of the minimum 35 minute assessment. RMR (kcal·d⁻¹) was calculated using the weir equation (38).

Total Daily Energy Expenditure (TDEE)/Non-Exercise Energy Expenditure (NEEx)—TDEE was assessed by doubly labeled water (DLW) over a 14-day period at baseline and 10 months. The end study assessment (10 months) was obtained during the final 2 weeks of the exercise training protocol. Participants reported to our laboratory between 8 and 9 a.m. after an overnight fast. Baseline urine specimens were collected from each participant prior to oral dosing with a mixed solution of ²H₂¹⁸O. The isotope given to each participant based on body weight (0.10g·kg⁻¹ of ²H₂O and 0.15g·kg⁻¹ H₂¹⁸O) and was followed with a rinse solution of 100ml of tap water. A weighed 1:400 dilution of each

participant's dose was prepared and a sample of the tap water was stored at -70°C for later analysis. Additional urine samples were collected on days 1 and 14. On these days two urine samples were collected at least three hours apart. All urine samples were stored in sealed containers at -70°C prior to analysis. Samples were analyzed in duplicate for $^2\text{H}_2\text{O}$ and H_2^{18}O by isotope ratio mass spectrometry as previously described by Herd et al. (15). Total daily energy expenditure (TDEE) was estimated using the equation of Elia (10): Total EE ($\text{MJ}\cdot\text{d}^{-1}$) = $(15.48/\text{RQ} + 5.55) \times \text{rCO}_2 (\text{L}/\text{d})$. NEEEx, i.e. energy expenditure not associated with exercise training, was calculated as $[(\text{TDEE} \times 0.9) - \text{RMR}] - \text{net EEEx} (\text{EEEx} - \text{RMR})$. This approach assumes that the thermic effect of food represents 10% of TDEE (39). EEEx for exercise sessions during the DLW assessment period was assessed by indirect calorimetry as described previously. The duration of exercise periods was obtained from exercise logs maintained by research staff and verified by HR monitor. Note: Net EEEx at baseline equals zero.

Non-Exercise Physical Activity (NEPA)/Sedentary time—NEPA was assessed by a portable accelerometer (Actigraph GT1M, Actigraph, LLC, Pensacola, FL). The GT1M is a small, lightweight ($3.8 \times 3.7 \times 1.8 \text{ cm}$; 27 g) uni-axial piezoelectric accelerometer which measures and records vertical accelerations from approximately 0.05g to 2.0g with a frequency response from 0.25 to 2.50 Hz reflected as activity counts per minute ($\text{cts}\cdot\text{min}^{-1}$). Accelerometers were worn on an elastic belt over the non-dominant hip for seven consecutive days at baseline, 3.5, 7 and 10 months. The data collection interval was set at one minute with a minimum of 10 hours constituting a valid monitored day. Three valid days were required to be included in the accelerometer analysis. Non-wear time was identified as 60 consecutive minutes with 0 $\text{cts}\cdot\text{min}^{-1}$, with allowance for 1–2 minutes of accelerometer counts between 0 and 100 (34). Data were downloaded using ActiGraph software and processed using a custom SAS program developed by our group. The NEPA data was obtained by removing accelerometer data over the duration of exercise sessions, which was identified via exercise logs maintained by research staff and verified by a HR monitor, from the daily accelerometer data. The NEPA measures were then created as the time spent in different levels of physical activity not including time spent in exercise prescribed by the intervention. We assessed both average $\text{cts}\cdot\text{min}^{-1}$ (raw and percent) and non-exercise time spent sedentary ($<100 \text{ cts}\cdot\text{min}^{-1}$) and in light ($100\text{--}2019 \text{ cts}\cdot\text{min}^{-1}$), moderate ($>3 \text{ METs}$, $2020\text{--}5999 \text{ cts}\cdot\text{min}^{-1}$) and vigorous PA ($>6 \text{ METs}$, $>5999 \text{ cts}\cdot\text{min}^{-1}$) (34). A mean of approximately 6 valid days of accelerometer data were available. The number of valid days did not differ by intervention group over the four assessment time points. There were no significant differences in wear time between groups or over time.

Statistical analysis

Analysis of variance (ANOVA) and *t*-tests were conducted to compare NEEEx, TDEE, and RMR between and within groups. Then, general linear modeling (GLM) was used to assess the effects of age, sex, group, and changes in weight and aerobic capacity on changes in NEEEx and TDEE. General linear mixed modeling (GMM) was used to examine differences between groups (group effect), changes over time (time effect), and group-by-time interaction for NEPA measures including average $\text{cts}\cdot\text{min}^{-1}$, and (raw and percent) time spent in sedentary, light, moderate, and vigorous PA. The raw or model-based group means

were pairwise compared using a Bonferroni-correction for inflation in Type I error. Statistical significance was determined at 0.05 alpha level, and all analyses were performed using SAS Software, version 9.3 (SAS Institute Inc., Cary, NC).

RESULTS

One hundred forty-one individuals were randomized to one of the three study groups. Ninety-two individuals (65.2%) complied with the study protocol and completed all assessments for the primary outcomes (i.e., weight, body composition). The baseline characteristics of the 92 completers are presented in Table 1. There were no significant difference in baseline descriptive characteristics (age, body weight, BMI, body composition, aerobic capacity) between the three study groups or between those individuals who completed the study and those who did not (9). Due to technical problems or failure to comply with the assessment protocols, this report includes DLW data from 83 participants at baseline (400 kcal·session⁻¹, *n*=34; 600 kcal·session⁻¹, *n*=34; control, *n*=15) and 79 participants at 10 months (400 kcal·session⁻¹, *n*=30; 600 kcal·session⁻¹, *n*=32; control, *n*=17) and accelerometer data from 92 participants at baseline (400 kcal·session⁻¹, *n*=37; 600 kcal·session⁻¹, *n*=37; control, *n*=18) and 86 participants at 10 months (400 kcal·session⁻¹, *n*=34; 600 kcal·session⁻¹, *n*=37; control, *n*=15). There were no differences in baseline characteristics or weight loss between those that completed all tests compared to those with missing data.

Energy Expenditure

A summary of the ANOVA and paired-samples *t*-test results for NEE_x, TDEE, and RMR are presented by group and sex in Table 2 and Figure 1.

NEE_x—There were no significant between or within group differences for change in NEE_x in the total sample, or in men and women. In the total sample, NEE_x increased in the 400 kcal·session⁻¹ group ($+16 \pm 511$ kcal·d⁻¹), decreased in the 600 kcal·session⁻¹ group (-37 ± 479 kcal·d⁻¹), and decreased in controls (-107 ± 667 kcal·d⁻¹). The patterns of change in NEE_x differed by sex. In men, NEE_x decreased in both the 400 (-66 ± 578 kcal·d⁻¹) and 600 kcal·session⁻¹ groups (-66 ± 533 kcal·d⁻¹) and was essentially unchanged in controls ($+11 \pm 758$ kcal·d⁻¹). In women, NEE_x increased in the 400 kcal·session⁻¹ group ($+92 \pm 445$ kcal·d⁻¹), was essentially unchanged in the 600 kcal·session⁻¹ group (-6 ± 432 kcal·d⁻¹) and decreased in controls (-263 ± 549 kcal·d⁻¹). Approximately, 50.0% of the participants in the 400 kcal group, 38% in the 600 kcal group and 44% in the control group increased NEE_x over the 10 month intervention.

RMR—There were no significant between or within group differences for change in RMR in the total sample or in men or women. RMR decreased in both the 400 and 600 kcal·session⁻¹ groups, reflecting exercise induced weight loss (~5%) (8) and was essentially unchanged in controls reflecting minimal weight gain in the control group (8).

TDEE—Results for change in TDEE varied by group and sex. In the total sample TDEE increased significantly from baseline to 10 months in the 600 kcal·session⁻¹ group ($+289 \pm 434$ kcal·d⁻¹). The increase in TDEE in the 400 kcal·session⁻¹ group ($+191 \pm 614$ kcal·d⁻¹)

and the decrease in TDEE in controls ($-111 \pm 588 \text{ kcal}\cdot\text{d}^{-1}$) were both non-significant. In men, there were no significant increases in TDEE in the 400 kcal-session⁻¹ ($+62 \pm 634 \text{ kcal}\cdot\text{d}^{-1}$), 600 kcal-session⁻¹ ($+215 \pm 510 \text{ kcal}\cdot\text{d}^{-1}$), and control groups ($+18 \pm 748 \text{ kcal}\cdot\text{d}^{-1}$), with no significant group differences for change in TDEE. In women, TDEE increased significantly in the 600 kcal-session⁻¹ group ($+368 \pm 336 \text{ kcal}\cdot\text{d}^{-1}$), and decreased significantly in controls ($-283 \pm 232 \text{ kcal}\cdot\text{d}^{-1}$). The increase in TDEE in the 400 kcal-session⁻¹ group ($+312 \pm 590 \text{ kcal}\cdot\text{d}^{-1}$) in women, while not statistically significant ($p=0.059$), is of potential clinical relevance.

General Linear Modeling

General linear models including age, sex, group, change in weight and change in aerobic capacity were examined to investigate the factors associated with changes in NEE_x and TDEE. Decreased weight from baseline to 10 months was significantly associated with increased NEE_x ($p=0.014$). Participant age was significantly positively associated with change in TDEE ($p=0.025$; e.g. greater increases in older participants) while change in weight ($p=0.097$), aerobic capacity ($p=0.084$), and group ($p=0.090$) were not.

General Linear Mixed Modeling

NEPA and Sedentary Time—As shown in Figure 2, NEPA (average cts·min⁻¹) decreased in controls and was essentially unchanged or slightly increased in the exercise intervention groups. There was a significant group-by-time interaction ($p=0.009$), with significantly higher NEPA in the 600 kcal-session⁻¹ group compared with controls at 7 months ($p<0.001$) and significantly higher NEPA in both the 400 ($p=0.043$) and 600 ($p<0.001$) kcal-session⁻¹ groups compared with control at 10 months. Results in men were similar to those in the total sample. In men, there was a significant group-by-time interaction ($p=0.008$), with significantly higher NEPA in the 600 kcal-session⁻¹ group vs. controls at 10 months ($p=0.014$). In women, there were no significant effects of group, time, and group-by-time interaction. Nevertheless, NEPA was significantly higher in the 600 kcal-session⁻¹ group vs. control at 3.5 ($p=0.013$), 7 ($p<0.001$) and 10 ($p=0.007$) months.

Figure 3 presents the minutes of NEPA spent in sedentary, light, moderate and vigorous intensity PA assessed by accelerometer. This analysis was also performed using the percentage of time in these activity categories after removing the time spent in exercise training. The results for these two approaches were the same; thus, we have presented NEPA results as min·day⁻¹ as they are more easily interpreted. There were no significant effects for group, time and group-by-time interaction for any intensity of PA. Nevertheless, sedentary time was significantly higher in the controls (model-based mean=609 min·d⁻¹) compared with the 600 kcal-session⁻¹ group (576 min·d⁻¹) at 7 months ($p=0.033$). Time spent in moderate NEPA in the 600 kcal-session⁻¹ (37 min·d⁻¹) was significantly greater than controls (29 min·d⁻¹) at 10 months ($p=0.048$). Approximately 79% of participants in the 400 kcal group, 54% in the 600 kcal group and 47% of controls decreased time spent in sedentary activity over the 10 month intervention. Approximately 47% of participants in the 400 kcal group, 57% in the 600 kcal group, and 40% of controls increased the time spent in NEPA (light + moderate + vigorous).

DISCUSSION

NEEx

We found no significant change in NEEx in a sample of initially sedentary, overweight and obese young adults, in response to a 5 d·wk⁻¹ aerobic exercise intervention (400 or 600 kcal·session⁻¹) over 10 months. Results from the limited number of studies where NEEx was assessed by DLW have reported increased (24), decreased (4, 13) and no change (40) in NEEx in response to aerobic exercise training. For example, Meijer *et al.* (24) reported a significant increase in NEEx in a small sample of adult men and women ($n=8$) who completed a 5-month training program in preparation to run a half-marathon. Using a cross-over design, Whybrow *et al.* (40) found no significant change in NEEx in a small sample ($n=12$) of normal/overweight adults who completed a 14-day exercise intervention at two levels of EEEx. In a non-randomized trial, Colley *et al.* (4) reported a significant decrease in NEEx in response to a 4-week supervised moderate intensity walking program (target EEEx = 1,500 kcal·wk⁻¹) in a small sample ($n=7$) of overweight/obese women (mean age = 41.1 years). Goran and Poehlman (13) also observed a significant reduction in NEEx in response to a 3 d·wk⁻¹, cycle ergometer exercise program (300 kcal·session⁻¹) in a small sample ($n=5$ women, $n=6$ men) of older adults (~65 years).

The majority of studies where NEEx has been estimated using other less precise techniques, including accelerometry (16), a combination of accelerometry and heart rate monitoring (35), heart rate monitoring with individual heart rate energy expenditure calibration (17, 21, 31) or SenseWear Pro arm band (5) have shown no change in NEEx in response to aerobic exercise training. However, Morio *et al.* (26) reported decreased NEEx assessed by a 7-day activity diary in response to moderate intensity cycle ergometer training (3 d·wk⁻¹, 14 weeks) in a small sample of older (~63 years) men and women ($n=8$ women, $n=5$ men). Thus, the results of the current study, which suggest no significant change in NEEx in response to aerobic exercise training, are in agreement with the preponderance of the literature.

Our results, as well as those of others, should be interpreted with caution. The four other studies that have reported on the change in NEEx assessed by DLW in response to aerobic exercise training were generally conducted using non-randomized designs, in small samples (range: 7 to 12 participants/study) of normal weight individuals (13, 24, 40). With the exception of the 5-month trial by Meijer *et al.* (24), these studies used relatively short exercise interventions (range: 14 days (40) to 8 weeks (13)) and did not include assessments of EEEx by indirect calorimetry, which are necessary for accurate estimates of NEEx.

NEPA

In agreement with our results for change in NEEx, we found no change in NEPA or minutes of NEPA spent in sedentary, light, moderate or vigorous activities, assessed by accelerometer, resulting from participation in aerobic exercise training. NEPA tended to decrease in controls and remain relatively stable over the 10 month intervention in both exercise groups. Interestingly, we found no evidence that participating in an aerobic exercise intervention results in increased time spent sedentary as measured by accelerometry. In fact,

sedentary time tended to increase in controls and decrease in the exercise groups resulting in between group differences at 7 ($p=0.021$) and 10 months ($p=0.019$).

Our finding of no change in NEPA in response to aerobic exercise training is in agreement with results several short-term studies (range: 2 to 16 days) (19, 20, 36) and randomized trials (range: 13 to 32 weeks) (3, 28, 29). However, significantly increased NEPA has been reported 48 hours after completing 60 minutes of high intensity interval treadmill walking (5 minutes at $6 \text{ km}\cdot\text{h}^{-1}$, 10% grade, 5 minutes at $6 \text{ km}\cdot\text{h}^{-1}$, 0% grade) in a sample of overweight and obese, sedentary, young adult men (2). Significantly decreased NEPA has been reported in two 12-week non-randomized trials in overweight, older men and women (22, 23). Both of these trials included a resistance training component in addition to aerobic exercise. Interestingly, several studies have demonstrated disagreement between NEPA and NEEEx results within the same study. For example, Meijer *et al.* (24) found no effect of aerobic exercise training on NEPA assessed by accelerometer in a sample of men ($n=16$) and women ($n=16$); but found a significant increase in NEEEx assessed by DLW in a sub-sample ($n=4$ men, $n=4$ women) as previously described. Colley *et al.* (4) also reported a discrepancy between NEPA assessed by accelerometer and NEEEx assessed by DLW in a small sample ($n=7$) of overweight/obese women in response to a 4-week moderate intensity walking program (goal of $1,500 \text{ kcal}\cdot\text{wk}^{-1}$). NEPA was unchanged while NEEEx decreased significantly from baseline to week four. Potential discrepancies between assessments of NEEEx and NEPA argue for the use of DLW assessed NEEEx when trying to evaluate the impact of exercise in the context of weight management.

Response to increased EEEx

Our observation of no significant difference for change in either NEEEx or NEPA in response to increased levels of EEEx (400 or $600 \text{ kcal}\cdot\text{session}^{-1}$) is in agreement with other reports in the literature. For example, results from short-term trials over 7-days (31, 32), which assessed NEEEx using HR monitoring with individual HR/energy expenditure calibration, and 14-days (40) with NEEEx assessed by DLW, have both shown no difference for change in NEEEx with increased levels of EEEx. Hallowell *et al.* (16), in an 8-month trial, found no between group differences for change in NEEEx assessed by accelerometer for participants randomized to non-exercise control or aerobic exercise at 5023 or $8272 \text{ kJ}\cdot\text{wk}^{-1}$. Church *et al.* (3) reported no significant between group difference for change in NEPA, assessed by pedometer, in a sample of older, overweight/obese women who completed a 6-month exercise intervention at energy expenditures of 4, 8, or $12 \text{ kcal}\cdot\text{kg}\cdot\text{wk}^{-1}$. In a sample of overweight/obese young adult men (age ~ 30 years), Rosenkilde *et al.* (29) reported no significant difference for change in NEPA, assessed by accelerometer, between men who completed an aerobic exercise intervention ($3 \text{ d}\cdot\text{wk}^{-1}$) at either 300 or $600 \text{ kcal}\cdot\text{session}^{-1}$. Although not statistically significant, NEPA was increased 37% ($p=0.09$) in the $300 \text{ kcal}\cdot\text{session}^{-1}$ group vs. control (29).

Individual variability

Although we observed no significant mean change, there was considerable inter-individual variability in the NEEEx and NEPA response to aerobic exercise training. Reductions in both NEEEx and NEPA were seen in approximately 50% of participants in the exercise groups.

Inter-individual variability in the response of both NEE_{Ex} and energy intake to exercise contribute to the high levels of inter-individual variability in the weight change response to aerobic exercise training (7, 25). The identification of both participant characteristics (e.g., age, sex, weight, race/ethnicity, aerobic capacity) and characteristics of the exercise intervention (e.g., mode, frequency, intensity, duration, time of day, level of EEEx) associated with decreased NEPA and NEE_{Ex} in response to aerobic exercise training will be important for the development of targeted, effective weight management interventions involving exercise alone or exercise combined with energy restriction.

TDEE

In this study TDEE was significantly increased in the 600 kcal·session⁻¹ groups, but not in the 400 kcal·session⁻¹ (Figure 1). TDEE increased even with weight loss over the 10 month intervention of -3.9 kg (-4.3%) in the 400 and -5.2 kg (-5.7%) in the 600 kcal groups (9). The increased TDEE observed in both exercise groups also occurred despite small decreases in RMR in both groups and small changes in NEE_{Ex} and reflected the increased daily EEEx when averaged over the 14-day DLW study period (400 kcal·session⁻¹ = 208 kcal·d⁻¹, 600 kcal·session⁻¹ = 324 kcal·d⁻¹). Previous studies where TDEE was assessed by DLW have reported both increased (24, 40) or no change (4, 13) in TDEE in response to aerobic exercise. Previous studies were completed over both short (14-days (40)), and longer durations (8 weeks (4, 13) to 20 weeks (24)) in generally small samples (range: 8 to 13 participants/study) of both normal weight (13, 24, 40) and overweight/obese individuals (4). We are unaware of other longer-term trials which have investigated the effect of increased EEEx on TDEE.

Sex differences

We observed potentially interesting sex differences for both change in TDEE and NEE_{Ex} in response to increased EEEx (Figure 1). In women, the change in TDEE in both the 400 and 600 kcal·session⁻¹ groups was greater than in men both the 400 and 600 kcal·session⁻¹ groups. The difference for change in TDEE was explained, at least in part, by the larger changes in both RMR and NEE_{Ex} in men compared to women. The literature on sex differences in the response of TDEE, NEE_{Ex} or NEPA in response to aerobic exercise training is limited. Fujita *et al.* (12), reported an increase in TDEE in response to a 25-week exercise intervention (three 2-hour supervised exercise classes·wk⁻¹) in a sample of older women (~67 years), but not in men. Stubbs *et al.* (31, 32) conducted two short-term cross-over studies, using nearly identical exercise protocols (control vs. two levels of cycle ergometer exercise) and assessments of NEE_{Ex} (HR monitoring) in small samples of normal weight men (*n*=6) (31) and women (*n*=6) (32). TDEE increased significantly with increased EEEx with no significant differences in NEE_{Ex} between exercise conditions and control. However, NEE_{Ex} decreased significantly over the 7-day protocol in men, but not in women (31, 32).

Strengths and Limitations

Strengths of the current study include the use of a randomized efficacy design with an intervention over 10-months that supervised exercise with two levels of EEEx, with

verification of EEEx and assessment of RMR by indirect calorimetry, TDEE measured by DLW, a relative large sample compared with the limited available literature, inclusion of both men and women, and the inclusion of measures of both NEEEx and NEPA. However, as previously described, MET-2 was not specifically designed or powered to detect between or within group or sex differences in the response of NEEEx or NEPA to aerobic exercise training. In addition, NEEEx was assessed only at baseline and the end of the study which precluded any assessment of the time course of change in NEEEx over the course of the 10-month intervention.

Summary

We found no significant change in mean NEEEx or NEPA in a sample of initially sedentary, overweight and obese young adults, in response to a 5 day·wk⁻¹ aerobic exercise intervention (400 or 600 kcal·session⁻¹) over 10 months. However, there was considerable inter-individual variability in the NEEEx and NEPA response. The change in NEEEx and NEPA did not differ significantly by level of EEEx; however, both NEEEx and NEPA tended to increase with increased EEEx. The observation of an increase in TDEE in both the 400 and 600 kcal·session⁻¹ groups that was greater in women than in men is interesting and warrants confirmation from an adequately powered trial. Our results, and those from the limited available literature (one short-term and three non-randomized trials), suggest the need for additional randomized trials using state-of-the art assessment techniques. Trials should be designed and powered to determine the effect of intervention factors including exercise mode, frequency, level of EEEx, intermittent vs. continuous exercise, exercise time of day, and participant factors including age, sex, race/ethnicity, body weight, and aerobic capacity on both TDEE and NEEEx. This information will be important in designing targeted interventions using exercise alone, or exercise in combination with energy restriction, for weight management.

Acknowledgments

This study was supported by the National Institutes of Health grant R01-DK049181.

The results of the present study do not constitute endorsement by ACSM.

REFERENCES

1. USDoHaH Services. , editor. 2008 Physical Activity Guidelines for Americans. Office of Disease Prevention & Health Promotion; 2008. <http://www.health.gov/paguidelines>
2. Alahmadi MA, Hills AP, King NA, Byrne NM. Exercise intensity influences nonexercise activity thermogenesis in overweight and obese adults. *Medicine and science in sports and exercise*. 2011; 43(4):624–631. [PubMed: 21412111]
3. Church TS, Martin CK, Thompson AM, Earnest CP, Mikus CR, Blair SN. Changes in weight, waist circumference and compensatory responses with different doses of exercise among sedentary, overweight postmenopausal women. *PloS one*. 2009; 4(2):e4515. [PubMed: 19223984]
4. Colley RC, Hills AP, King NA, Byrne NM. Exercise-induced energy expenditure: implications for exercise prescription and obesity. *Patient education and counseling*. 2010; 79(3):327–332. [PubMed: 20392589]
5. Di Blasio A, Ripari P, Bucci I, et al. Walking training in postmenopause: effects on both spontaneous physical activity and training-induced body adaptations. *Menopause*. 2012; 19(1):23–32. [PubMed: 21993080]

6. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW, Smith BK. American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. *Medicine and science in sports and exercise*. 2009; 41(2):459–471. [PubMed: 19127177]
7. Donnelly JE, Hill JO, Jacobsen DJ, et al. Effects of a 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women: the Midwest Exercise Trial. *Arch Intern Med*. 2003; 163(11):1343–1350. [PubMed: 12796071]
8. Donnelly JE, Honas JJ, Smith BK, et al. Aerobic exercise alone results in clinically significant weight loss for men and women: midwest exercise trial 2. *Obesity (Silver Spring, Md)*. 2013; 21(3):E219–E228.
9. Donnelly JE, Washburn RA, Smith BK, et al. A randomized, controlled, supervised, exercise trial in young overweight men and women: the Midwest Exercise Trial II (MET2). *Contemporary clinical trials*. 2012; 33(4):804–810. [PubMed: 22504223]
10. Elia, M. Converting carbon dioxide production to energy expenditure. In: Prentice, AM., editor. *The doubly-labeled water method for measuring energy expenditure. Technical recommendations for use in humans. A consensus report by the IDECG working group*. Vienna: NAHRES-4; 1990. p. 193-211.
11. Epstein LH, Wing RR. Aerobic exercise and weight. *Addictive Behaviors*. 1980; 5(4):371–388. [PubMed: 7211534]
12. Fujita K, Nagatomi R, Hozawa A, et al. Effects of exercise training on physical activity in older people: a randomized controlled trial. *Journal of epidemiology / Japan Epidemiological Association*. 2003; 13(2):120–126. [PubMed: 12675121]
13. Goran MI, Poehlman ET. Endurance training does not enhance total energy expenditure in healthy elderly persons. *American Journal of Physiology-Endocrinology And Metabolism*. 1992; 263(5):E950–E957.
14. Haugen HA, Melanson EL, Tran ZV, Kearney JT, Hill JO. Variability of measured resting metabolic rate. *The American journal of clinical nutrition*. 2003; 78(6):1141–1145. [PubMed: 14668276]
15. Herd S, Vaughn W, Goran M. Comparison of zinc reduction with platinum reduction for analysis of deuterium-enriched water samples for the doubly-labeled water technique. *Obes Res*. 1999; 8(4):302–308. [PubMed: 10933306]
16. Hollowell RP, Willis LH, Slentz CA, Topping JD, Bhakpar M, Kraus WE. Effects of exercise training amount on physical activity energy expenditure. *Medicine and science in sports and exercise*. 2009; 41(8):1640–1644. [PubMed: 19568195]
17. Keytel LR, Lambert MI, Johnson J, Noakes TD, Lambert EV. Free living energy expenditure in post menopausal women before and after exercise training. *International Journal of Sports Nutrition and Exercise Metabolism*. 2001; 11:226–237.
18. King NA, Caudwell P, Hopkins M, et al. Metabolic and behavioral compensatory responses to exercise interventions: barriers to weight loss. *Obesity (Silver Spring, Md)*. 2007; 15(6):1373–1383.
19. Koulouri AA, Tigbe WW, Lean ME. The effect of advice to walk 2000 extra steps daily on food intake. *Journal of human nutrition and dietetics : the official journal of the British Dietetic Association*. 2006; 19(4):263–266. [PubMed: 16911238]
20. Lynch KB, Corbin CB, Sidman CL. Testing compensation: does recreational basketball impact adult activity levels? *Journal of physical activity & health*. 2009; 6(3):321–326. [PubMed: 19564660]
21. McLaughlin R, Malkova D, Nimmo MA. Spontaneous activity responses to exercise in males and females. *European journal of clinical nutrition*. 2006; 60(9):1055–1061. [PubMed: 16493451]
22. Meijer E, Westerterp K, Verstappen F. Effect of exercise training on physical activity and substrate utilization in the elderly. *International journal of sports medicine*. 2000; 21(7):499–504. [PubMed: 11071053]
23. Meijer EP, Westerterp KR, Verstappen FT. Effect of exercise training on total daily physical activity in elderly humans. *European journal of applied physiology and occupational physiology*. 1999; 80(1):16–21. [PubMed: 10367718]

24. Meijer GA, Janssen GM, Westerterp KR, Verhoeven F, Saris WH, ten Hoor F. The effect of a 5-month endurance-training programme on physical activity: evidence for a sex-difference in the metabolic response to exercise. *European journal of applied physiology and occupational physiology*. 1991; 62(1):11–17. [PubMed: 2007389]
25. Melanson EL, Keadle SK, Donnelly JE, Braun B, King NA. Resistance to exercise-induced weight loss: compensatory behavioral adaptations. *Medicine and science in sports and exercise*. 2013; 45(8):1600–1609. [PubMed: 23470300]
26. Morio B, Montaurier C, Pickering G, et al. Effects of 14 weeks of progressive endurance training on energy expenditure in elderly people. *British journal of Nutrition*. 1998; 80:511–519. [PubMed: 10211049]
27. Potteiger JA, Kirk EP, Jacobsen DJ, Donnelly JE. Changes in resting metabolic rate and substrate oxidation after 16 months of exercise training in overweight adults. *Int J Sport Nutr Exerc Metab*. 2008; 18(1):79–95. [PubMed: 18272935]
28. Rangan VV, Willis LH, Slentz CA, et al. Effects of an 8-month exercise training program on off-exercise physical activity. *Medicine and science in sports and exercise*. 2011; 43(9):1744–1751. [PubMed: 21364488]
29. Rosenkilde M, Auerbach P, Reichkender 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. *American Journal of Physiology - Regulatory Integrative and Comparative Physiology*. 2012; 303(6):R571–R579.
30. Stiegler P, Cunliffe A. The role of diet and exercise for the maintenance of fat-free mass and resting metabolic rate during weight loss. *Sports medicine*. 2006; 36(3):239–262. [PubMed: 16526835]
31. Stubbs RJ, Sepp A, Hughes DA, et al. The effect of graded levels of exercise on energy intake and balance in free-living men, consuming their normal diet. *European journal of clinical nutrition*. 2002; 56:129–140. [PubMed: 11857046]
32. Stubbs RJ, Sepp A, Hughes DA, et al. The effect of graded levels of exercise on energy intake and balance in free-living women. *International journal of obesity and related metabolic disorders: journal of the International Association for the Study of Obesity*. 2002; 26(6):866–869.
33. Taylor H, Jacobs D, Schucker B, Knudsen J, Leon A, Debacker G. A questionnaire for the assessment of leisure time physical activities. *J Chronic Dis*. 1978; 31:741–755. [PubMed: 748370]
34. Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. *Medicine and science in sports and exercise*. 2008; 40(1):181–188. [PubMed: 18091006]
35. Turner JE, Markovitch D, Betts JA, Thompson D. Nonprescribed physical activity energy expenditure is maintained with structured exercise and implicates a compensatory increase in energy intake. *The American journal of clinical nutrition*. 2010; 92(5):1009–1016. [PubMed: 20826629]
36. Washburn RA, Ficker JL. Does participation in a structured high-intensity exercise program influence daily physical activity patterns in older adults? *Research quarterly for exercise and sport*. 1999; 70(2):201–205. [PubMed: 10380252]
37. Washburn RA, Lambourne K, Szabo AN, Herrmann SD, Honas JJ, Donnelly JE. Does Increased Prescribed Exercise Alter Non-Exercise Physical Activity/Energy Expenditure in Healthy Adults? A Systematic Review. *Clinical Obesity*. In Press.
38. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. *J Physiol*. 1949; 109(1–2):1–9. [PubMed: 15394301]
39. Weststrate JA. Resting metabolic rate and diet-induced thermogenesis: a methodological reappraisal. *Am.J.Clin.Nutr*. 1993; 58:592–601. [PubMed: 8237862]
40. Whybrow S, Hughes DA, Ritz P, et al. The effect of an incremental increase in exercise on appetite, eating behaviour and energy balance in lean men and women feeding ad libitum. *The British journal of nutrition*. 2008; 100(5):1109–1115. [PubMed: 18377694]

Figure 1.

Change in energy expenditure (NEEx, RMR, TDEE) from month 0 to month 10 by group and sex. NEEx = Non-exercise energy expenditure, RMR = Resting metabolic rate, TDEE = Total daily energy expenditure. Error bars represent standard errors.

Figure 2. Mean accelerometer activity cts·min⁻¹ at months 0, 3.5, 7, and 10 by group and sex. Error bars represent standard errors.

Figure 3. Time spend sedentary and in light, moderate and vigorous activity at months 0, 3.5, 7, and 10 by group and sex. Error bars represent standard errors.

Table 1

Baseline sample characteristics

Variable	Study Groups		
	400 kcal·session ⁻¹ (n=37)	600 kcal·session ⁻¹ (n=37)	Control (n=18)
Age (yrs.)	23.1 (3.0)	23.0 (3.5)	22.6 (3.0)
Height (cm)	169.7 (10.0)	172.4 (10.1)	170.5 (9.7)
Weight (kg)	91.4 (20.7)	92.0 (16.1)	87.4 (14.6)
BMI (kg·m ⁻²)	31.2 (5.6)	30.6 (3.9)	29.7 (3.8)
Body fat (%)	39.6 (7.5)	40.2 (6.2)	41.0 (6.1)
Women (%)	51.4	48.6	50.0

Note. Values are mean (SD) unless otherwise stated. There were no significant differences in demographic characteristics or for the percentage of women participants across the 3 study groups (all $p>0.05$).

Table 2

Change in total daily energy expenditure (TDEE), resting metabolic rate (RMR), and non-exercise energy expenditure (NEEx) over 10 months by intervention group and sex.

	Study Groups						Between-group difference
	400 kcal·session ⁻¹			600 kcal·session ⁻¹			
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	
<i>Total Sample</i>							
TDEE (kcal·d ⁻¹)							
Baseline	34	2851 (624)	34	3007 (705)	15	2710 (580)	0.311
10 months	30	3072 (624)	32	3229 (696)	17	2736 (740)	0.060
Change	29	191 (614)	29	289 (434)	14	-111 (588)	0.082
Within group (<i>p</i> -value)		0.104		0.001		0.493	
RMR (kcal·d ⁻¹)							
Baseline	34	1759 (377)	34	1826 (355)	15	1626 (263)	0.190
10 months	30	1726 (347)	32	1754 (348)	17	1651 (326)	0.606
Change	29	- 50 (212)	29	-26 (221)	14	7 (255)	0.742
Within group (<i>p</i> -value)		0.218		0.528		0.925	
NEEx (kcal·d ⁻¹)							
Baseline	34	807 (362)	34	881 (406)	15	813 (394)	0.708
10 months	30	832 (408)	32	829 (452)	17	811 (539)	0.998
Change	29	16 (511)	29	-37 (479)	14	-107 (667)	0.776
Within group (<i>p</i> -value)		0.869		0.683		0.560	
<i>Men</i>							
TDEE (kcal·d ⁻¹)							
Baseline	17	3151 (565)	19	3408 (540)	8	2970 (624)	0.154
10 months	15	3253 (643)	15	3700 (571)	9	3126 (628)	0.056
Change	14	62 (634)	15	215 (510)	8	18 (748)	0.708
Within group (<i>p</i> -value)		0.719		0.126		0.947	
RMR (kcal·d ⁻¹)							
Baseline	17	1982 (311)	19	2059 (215)	8	1777 (167)	0.037*

	Study Groups							Between-group difference <i>p</i> -value	
	400 kcal·session ⁻¹			600 kcal·session ⁻¹			Control		
	N	Mean (SD)		N	Mean (SD)		Mean (SD)		
10 months	15	1933 (264)		15	2038 (245)		9	1809 (233)	0.110
Change	15	-88 (179)		15	-43 (195)		8	6 (121)	0.490
Within group (<i>p</i> -value)		0.090			0.405			0.899	
NEEx (kcal·d ⁻¹)									
Baseline	17	854 (327)		19	1008 (414)		8	897 (418)	0.473
10 months	15	783 (413)		15	990 (466)		9	1005 (602)	0.414
Change	14	-66 (578)		15	-66 (533)		8	11 (758)	0.951
Within group (<i>p</i> -value)		0.674			0.642			0.969	
Women									
TDEE (kcal·d ⁻¹)									
Baseline	17	2551 (541)		15	2449 (549)		7	2412 (370)	0.838
10 months	15	2980 (567)		17	2814 (510)		8	2298 (622)	0.503
Change	15	312 (590)		14	368 (336)		6	-283 (232)	0.016**
Within group (<i>p</i> -value)		.0599			0.0013			0.034	
RMR (kcal·d ⁻¹)									
Baseline	17	1535 (299)		15	1531 (267)		7	1455 (254)	0.798
10 months	15	1519 (297)		17	1504 (201)		8	1474 (336)	0.929
Change	15	-14 (239)		14	-8 (252)		6	8 (386)	0.986
Within group (<i>p</i> -value)		0.823			0.908			0.962	
NEEx (kcal·d ⁻¹)									
Baseline	17	760 (398)		15	719 (344)		7	716 (372)	0.940
10 months	15	880 (412)		17	686 (401)		8	595 (381)	0.216
Change	15	92 (445)		14	-6 (432)		6	-263 (549)	0.289
Within group (<i>p</i> -value)		0.434			0.961			0.294	

Note.

* 600 group different than Control group.
** 400 and 600 different than Control group.