A Rapidly Occurring Compensatory Decrease in Physical Activity Counteracts Diet-Induced Weight Loss in Female Monkeys

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Running Head: Decrease in Activity Counteracts Weight Loss

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Abstract

To study changes in energy balance occurring during the initial phases of dieting, eighteen adult ovariectomized female monkeys were placed on a low-fat diet and available calories were reduced by 30% as compared to baseline consumption for one month. Surprisingly, there was not significant weight loss, however daily activity level (measured by accelerometry) decreased soon after diet initiation and reached statistical significance by the fourth week of dieting (18±5.6% decrease, p=0.02). During a second month of dieting, available calories were reduced by 60% as compared to baseline consumption, leading to 6.4±1.7% weight loss, and further suppression of activity. Metabolic rate decreased by 68±12 kcal/day; with decreased activity accounting for 41±9 kcal/day, and the metabolic activity of the weight lost accounting for 21±5 kcal/day. A second group of 3 monkeys was trained to run on a treadmill for 1 hr/day, 5 days/week at 80% maximal capacity, leading to increased calorie expenditure of 69.6±10.7 kcal/day (equivalent to 49 kcal/day for 7 days). We conclude that a diet-induced decrease in physical activity is the primary mechanism the body uses to defend against diet-induced weight loss, and undertaking a level of exercise that is recommended to counteract weight gain and promote weight loss is able to prevent the compensatory decrease in physical activity-associated energy expenditure that slows diet-induced weight loss.

Keywords: Obesity, calorie reduction, activity
Introduction

Moderate weight loss in obese and overweight individuals is associated with major health benefits, including reductions in the risk of heart disease (37), stroke (37), type 2 diabetes (35, 42, 70), hypertension (18, 49), hyperlipidemia (21, 60), hypercholesterolemia (22, 60), cardiovascular disease (22, 60), osteoarthritis (60), and depression (22, 60). Thus, it is not surprising that at any time two-thirds of obese North American adults are attempting to lose weight (58, 61). Currently, American consumers spend $33 billion annually on weight loss products and services (10). Despite these efforts, the prevalence of overweight and obese adults has escalated over the past several decades, such that 65% of adults in the United States have a Body Mass Index (BMI) above the healthy range (19). An important contributing factor to the increasing prevalence of obesity is that most of the individuals attempting to lose weight are unsuccessful (60, 63). Dieting is currently the most common weight loss strategy (14, 29, 31, 41, 81). However, the success rates for diet-induced weight loss are very low, ranging from 2 to 20% of individuals actually maintaining weight loss (30, 62, 72, 82). Weight loss in response to a diet is difficult to accomplish and maintain as compensatory mechanisms act to prevent weight loss by decreasing energy expenditure (5, 11-13, 26, 43).

The majority of studies examining diet-induced weight loss in humans have not directly measured physical activity or food intake, but rather have relied upon self-report of these measures (28, 50, 71, 83), which has been shown to be unreliable (7, 28, 34, 44, 46, 69). There is clear evidence that dieting leads to a compensatory decrease in total metabolic rate in humans (5, 11-13, 26, 43) and nonhuman primates (38). It has been postulated that a decrease in physical activity contributes to the overall decrease in energy expenditure accompanying calorie reduction and that this reduction in physical activity is at least partially responsible for the decreased effectiveness of dieting to promote weight loss. Evidence to support this hypothesis comes from several studies that suggest that people decrease physical activity level in response
to reduced calorie consumption (13, 33, 43, 55). Also, a single report directly measured physical activity prior to and after a dietary weight loss intervention in women and found that physical activity decreased after the weight loss intervention (74). However, this study measured activity for short periods of time (5-6 days) and accelerometers were removed during periods of the day when individuals were sleeping or bathing. In contrast in rodents, detailed measurements of physical activity indicate that activity increases in response to calorie reduction (8, 17, 45, 57). It is hypothesized that the increase in activity in rodent models reflects an increased drive to forage for food, as the elevated activity is decreased when food is made available (36). It is likely that the differential regulation of physical activity in response to calorie reduction in humans versus rodents is due to species differences in stored energy.

To examine the compensatory decreases in energy expenditure that occur in response to diet-induced weight loss in detail we have studied a primate species that shows metabolic regulation similar to humans (23, 73) (i.e., rhesus monkeys). A group of eighteen ovariectomized adult female rhesus monkeys was put on a carefully controlled diet for two months and food intake, physical activity, total metabolic rate and body composition were measured prior to and over the course of two months of dieting, a first month in which available calories were reduced by 30% as compared to baseline consumption and a second month in which available calories were reduced by 60% as compared to baseline consumption.

**Materials and Methods**

**Animals**

Twenty one adult female rhesus monkeys (*Macaca mulatta*), 9-13 years of age, were used in this study.

For Experiment 1, 18 monkeys were housed in individual stainless steel cages (32 x 24 x 27 or 32 x 34 x 27 in.) in a temperature-controlled room (24 ± 2 C), with lights on between 0700 and 1900 h. Two and a half years prior to the initiation of this study, these monkeys were
ovariectomized and placed on a diet higher in fat than standard monkey chow (35% of calories from fat) to approximate the conditions experienced by many post-menopausal women in the Western world (77). This diet was formulated at the Oregon National Primate Research Center (ONPRC) following a modification of the recipe developed by Clarkson and colleagues to study diet-induced atherosclerosis (59, 77). The diet utilized in this study was modified to prevent loose stool by lowering the percent fat from 43 to 35%, increasing the amount of carbohydrate from 39 to 46% and reducing the amount of calcium and phosphorus. The diet had a wheat flour base and 35% of calories were derived from fat, 19% from protein, and 46% from carbohydrate. At the beginning of this study, during a one-month baseline period, monkeys continued to receive high-fat diet *ad libitum*. After the baseline period, monkeys were placed on monkey chow (5% fat) which involved switching their food back to the standard feeding regimen at ONPRC in which they received high protein monkey chow biscuits (no. 5047, jumbo biscuits, Ralston Purina Co., St. Louis, MO; approximately 16.5 g each, 3.11 metabolizable kcal/g, 616 kcal/meal, 25% protein, 5% fat, 6.5% fiber, 6% ash and 3% nutrients). During the first month of the diet, the number available calories were reduced by 30% as compared to baseline consumption. During the second month of the diet, calories available were reduced by 60% as compared to baseline calorie consumption. Throughout the study, two meals a day were provided at 0915 and 1515 h. All aspects of the study were reviewed and approved by the ONPRC Animal Care and Use Committee.

For Experiment 2, three adult female monkeys 13-14 years of age lived in social groups in pens measuring 14 x 11 x 10 ft, which had perches at various heights and various toys available. Skylights provided natural lighting supplemented with artificial lighting from approximately 0730 to 1600 h each day. Temperature was maintained at 24±3 C. Monkeys were fed Purina high protein monkey chow (no. 5045; Ralston Purina, St. Louis, MO) supplemented with seeds, fresh fruit and vegetables. Monkeys were trained to enter transfer cages from their home pen so that they could be transported to a different room for running on
treadmills during the experiment. All aspects of the study were reviewed and approved by the University of Pittsburgh Animal Care and Use Committee.

Experimental Design

Experiment 1:

The overall goal of this study was to examine the compensatory mechanisms that counteract diet-induced weight loss. During the baseline period (1 month), initial measurements of body weight, body composition, food intake, activity, total energy expenditure, basal metabolic rate, thermic effect of food and activity-associated energy expenditure were made. Monkeys were subsequently placed on a diet for two months. In the first month of the study, available calories were reduced by 30% as compared to baseline consumption. In the second month of the study, calorie intake was reduced by 60% as compared to baseline consumption. A second measurement of body composition, total energy expenditure, basal metabolic rate, thermic effect of food and activity-associated energy expenditure was made at the end of the second month of dieting. Throughout the study, food intake was measured at every meal, body weight was measured weekly, and activity was measured continuously via accelerometry.

Experiment 2:

The overall goal of this study was to examine the change in daily activity that occurs when animals participate in an exercise program of one hour of running a day, 5 days/week, at levels recommended by the American College of Sports Medicine to prevent weight gain and promote weight loss (15). Monkeys wore collars with a small metal box attached, housing an omnidirectional accelerometer (Actical accelerometer, Respironics Inc., Phoenix, AZ) throughout the entire study to measure daily level of physical activity. After a baseline period, monkeys were trained to run on motor-driven treadmills and ran for one hour per day at 80% maximal capacity for 5 days/week for 12 weeks.
Experimental Measures

Food Intake: Total food consumption at each meal was recorded daily throughout the study, by counting the amount of food remaining prior to the next meal.

Body weight: Body weight measurements were made weekly prior to consumption of the AM meal, at approximately 0800 h.

DEXA-measurements: Percent body fat, percent central fat, percent peripheral fat, fat mass in grams and lean tissue mass in grams were determined using dual energy X-ray absorptiometry (DEXA) as previously described (64, 66). Animals were sedated with Telazol (3 mg/kg; IM, Fort Dodge Animal Health, Fort Dodge, IA), supplemented with Ketamine HCL (10-20 mg/kg, IM.; Ketaset, Fort Dodge Animal Health, Fort Dodge, IA), and were positioned supine on the bed of a Lunar DPX scanner (Lunar Corporation, Madison, WI). Total body scans were done in the “Pediatric Medium” scan mode with a voltage of 76 kV. Lunar software version 3.4 was used to calculate body composition. Two or three scans were performed for each monkey at the initiation of the baseline period and after two months of dieting and averages were calculated for each measure. To delineate central fat mass from peripheral fat mass, fat in the trunk (including both the subcutaneous and visceral compartments), and fat in the extremities was calculated using standard methodology (9, 68).

Metabolic Rate: Metabolic rate was measured by placing each monkey in a sealed Lexan metabolic chamber (Columbus Instruments, Columbus, OH) and measuring the amount of carbon dioxide produced and oxygen consumed over a 24 hour period using a computer-controlled indirect open circuit calorimeter (Oxymax System, Columbus Instruments, Columbus, OH) and previously published methods (66). The metabolic chamber was approximately the same size as the monkey’s home cage (inside dimensions of 30” x 24” x 24”). In order to prevent social isolation stress during metabolic testing, two familiar monkeys (i.e., two monkeys routinely housed across the room from the experimental monkey) were placed in plain view of the subject. The metabolic rate of each monkey was assessed during the baseline period,
when monkeys were consuming high fat diet, and after two months of dieting. To determine total daily energy expenditure, monkeys were placed in the metabolic chamber at 1000 h and remained in the chamber until 0900 h the next morning. Before placement in the chamber monkeys were fed their standard meal at 0915 h. They were then fed a banana (114 g ± 10g, 108 calories) at 1515 h while in the chamber. Water was available ad libitum throughout metabolic testing. BMR was calculated as the average number of kilocalories expended per hour from 2300 to 0300 h. This time period was selected because this is when monkeys typically sleep, and heart rate (J Cameron, unpublished observations) and activity are lowest at this time of night (66).

**Activity:** Activity was measured continuously throughout the experiment using omnidirectional Actical accelerometers (Respironics, Phoenix, AZ) and previously published methods (66). Each monkey was fitted with a loose-fitting metal collar (Primate Products, Inc.; Immokalee, FL) that had an activity monitor, housed in a snug protective stainless steel box, mounted on it. The monitor was programmed to store the total number of activity counts per minute. During the study period monkeys were sedated with ketamine hydrochloride (10-20 mg/kg, IM; Ketaset, Fort Dodge Animal Health, Fort Dodge, IA) and the data from each activity monitor was downloaded at least every 45 days (the maximum number of days that the monitor can store data). After the data was downloaded and saved, the activity monitor was reprogrammed and replaced on the collar in order to resume collection of activity data. The monkeys in this study had been acclimated to wearing collars with activity monitors attached for over 6 months prior to the collection of measurements for this study. Average activity during the light and dark cycle was calculated for the baseline period and each week of the diet. Activity-associated energy expenditure was calculated using a previously published calculation of the amount of energy expended (in kcal) per activity count (66). This was calculated by measuring total energy expenditure at times of day in which there would be little contribution of the thermic effect of food to the total metabolic rate (from 1400 to 1500 and 1800 to 1900), subtracting basal
metabolic rate, and dividing the remaining energy expenditure by the number of activity counts occurring during this time period. The number of calories expended per activity count was multiplied by total daily activity counts to determine daily activity-associated energy expenditure.

**Exercise Training:** Monkeys were trained to run on a standard human size treadmill (Model 910e, Precor, Inc., Bothell, WA), using previously published techniques (78-80). Each treadmill was covered by a Plexiglas box that had numerous air holes in the front and back panels for adequate ventilation. Initially, for several days, the monkeys were acclimated to the treadmill by sitting on it and being allowed to explore the treadmill belt and the Plexiglas box. Monkeys then learned to walk on the treadmill and then speed and duration of each running session was slowly increased to 1.6 mph for 20 min/day. The treadmill adaptation period lasted 3-4 weeks. Subsequently, each monkey underwent a max test, and their target exercise level was individually determined as 1 hour of running, 5 days a week, at 80% of their maximal capacity. Monkeys were trained by gradually increasing speed and duration of each running session until they reached their individual target speed. Each monkey’s target amount of running was adjusted after a second max test, performed in week 7 of the study, so that they continued to train at 80% maximal capacity.

**Maximal Heart Rate Test Procedures:** After monkeys were trained to walk on the treadmill, and again after 7 weeks of running, each monkey had a maximal aerobic power test (max test) performed. Prior to the max test monkeys were adapted to wearing nylon jackets that would protect EKG electrodes and leads for several days. For electrode placement, monkeys were sedated with 0.1 mg/kg ketamine hydrochloride (Ketaject, Phoenix Pharmaceuticals Inc., St. Joseph, MO) and standard pediatric heart rate electrodes with self-adhesive pads were adhered to the monkey’s chest. The distal ends of the electrodes were attached to a TM8 telemetry transmitter (Life Sensing Instruments, Tullahoma, TN) that was placed in an inside pocket of a jacket that the monkeys wore to prevent them from manipulating the heart rate electrodes and transmitter. The heart rate signal was received by a HST 220
telemetry receiver (Life Sensing Instruments) and recorded by a computer. Software for the heart rate data collection and storage (Samsedate Heart Rate Variability System) was developed by Autrec, Inc. (Winston-Salem, NC).

For testing, heart rate was recorded while the monkey sat on the treadmill. Running was then initiated at a speed of 0.8 miles per hour (mph; 1.28 km/h) and speed was increased by 0.2 mph every 2 min until the monkey was no longer able to keep pace with the treadmill. Heart rate was recorded for six seconds at the end of each speed interval. Once the monkey reached maximum speed the treadmill was stopped briefly and then running was reinitiated at 0.8 mph for a five-minute recovery period. Heart rate was recorded at 1, 3 and 5 min during the recovery period.

Statistical Analyses

For all analyses, normality and homoscedacity were initially tested. If these criteria were met, a repeated measures ANOVA was utilized to look at differences in variables over time. The assumption of sphericity was examined with Mauchly's Test. The Greenhouse-Geiser correction factor was used in cases where the assumption of sphericity was violated. Least Significant Difference post-hoc tests were used to determine time periods that were significantly different from each other. If the variables were measured twice then a paired t-test was used to look for differences in the variable before and after dieting. Correlations were determined using a Pearson product moment correlation. If data was not normally distributed, and could not be normalized by transformation (using a square root or log transformation) then nonparametric tests were utilized. To look for differences in non-normally distributed data over time the Friedman test was used, followed by the Wilcoxon Signed Ranks test. If variables were measured twice, then a Wilcoxon Signed Ranks test was utilized. A Spearman’s rho correlation was used to analyze relationships between parameters that were not normally distributed. Data are presented as mean ± SEM. Alpha values are considered significant with p ≤ 0.05. All
statistical analyses were conducted using the SPSS software package, version 13.0 (SPSS Inc., Chicago, Illinois).

Results

During the first month of dieting available calories were reduced by 30% as compared to baseline consumption and the percent of calories from fat in the diet was reduced from 35 to 5 percent. During this one-month period several monkeys ate fewer calories than provided (possibly due to differences in palatability and texture between the diets) so the actual percent decrease in calorie intake was 44±2.6%. At the beginning of the second month of dieting, available calories were reduced by 60% as compared to baseline consumption. A few monkeys continued to eat less food than provided so that the actual average percent reduction of caloric intake was 68±0.81%.

After one month of dieting, there was no significant weight loss (p=0.55). Body weight was significantly reduced by dieting (F1,85,31.5=19.41, p<0.0001) during the seventh (p=0.003) and eighth (p<0.0001) weeks of the dieting (Figure 1A). The average percent of weight loss over the two-month diet was 6.4 ± 1.7%.

Body composition was measured by DEXA scan at baseline and at the end of the two month diet period. On average, fat mass decreased from 1780 ± 365 grams to 1568 ± 297 grams (t=2.3, df=15, p=0.04; Table 1) and lean tissue mass from 5483 ± 223 grams to 5276 ± 225 grams (t=2.4, df=15, p=0.03; Table 1) during the two-month diet. However, dieting did not change percent body fat (p=0.28; Table 1) or body fat distribution [as the percent of fat distributed centrally (p=0.36) and peripherally (p=0.23) did not change; Table 1].

In contrast to weight loss, daily activity level began to decrease soon after placement on the diet (F3,4 47.4=5.13, p=0.03; Figure 1B) and was significantly decreased by the end of the fourth week of dieting (18±5.6% decrease in activity, p=0.02). During the second month of dieting, physical activity was further suppressed (26±7.6% decrease in activity, p<0.0001).
In response to the decrease in available calories, total daily energy expenditure decreased by 68±12 kcal/day by the end of two months of dieting (t=5.3, df=15, p<0.0001; Figure 2A). Activity-associated energy expenditure significantly decreased by 41±9 kcal/day (t=-5.5, df=16, p<0.0001; Figure 2B). The loss of metabolically active tissue due to dieting accounted for a decrease in energy expenditure of 21±5 kcal/day. Dieting did not affect the thermic effect of an isocaloric meal (p=0.81; data not shown) or respiratory quotient (p=0.20; data not shown).

To determine if participating in a regular exercise program that is generally recommended to prevent weight gain and promote weight loss (15) would be able to counteract the diet-induced decrease in physical activity, three additional adult female rhesus monkeys were trained to run on a treadmill at 80% maximal capacity for 1 hr/day, 5 days/week, for three months. Participating in this exercise program was calculated to increase daily calorie expenditure by 69.6±10.7 kcal/day (t=-5.82, df=2, p=0.03, equivalent to 49 kcal/day for a seven day week; Figure 3A). The exercising monkeys experienced an average of a 6.1±1.2 percent weight loss during the three-month exercise period. Exercising for an hour a day did not significantly change total activity during the other 23 hours of the day (t=-0.39 df=2, p=0.74; Figure 3B).

Discussion

In this study, we characterized the compensatory decreases in activity and metabolic rate that accompany the initial stages of diet-induced weight loss in a nonhuman primate model of post-menopausal women. During the first month of dieting, no significant weight loss occurred, however daily physical activity level of the monkeys rapidly decreased after diet initiation and was significantly lower during the fourth week of dieting (18±5.6% decrease). During the second month of dieting, physical activity was further suppressed (26±7.6% decrease), and by the end of the second month of dieting monkeys had lost a significant amount
of weight (6.4±1.7% of initial weight), however it was minimal considering the substantial diet that they had been on for two months. A compensatory decrease in total energy expenditure (13% decrease) occurred in response to the diet, similar in magnitude to what has been previously reported in humans during dieting (12, 13, 26, 43, 75). Two thirds of the decrease in energy expenditure resulted from the decrease in level of physical activity, and in a second study we showed a similar amount of calories is expended by undertaking a moderate exercise routine of running 5 hours a week, at a level recommended by the American College of Sports Medicine to prevent weight gain and promote weight loss (25). Thus, we conclude that diet-induced decreases in level of physical activity is the primary mechanism the body uses to defend against diet-induced weight loss, and undertaking an exercise program of five hours of running per week is able to prevent the compensation in physical activity-induced calorie expenditure that slows diet-induced weight loss.

Activity-associated energy expenditure was reduced after two months of dieting due to both the decrease in movement (i.e. amount and intensity of activity), and because it takes less energy to move a reduced body weight (1, 2). This finding supports previous reports in rhesus monkeys (32, 54) and humans (13, 33, 43, 74) that report a decrease in physical activity accompanying reductions in calorie intake. In contrast, rodents show an increase in activity in response to calorie reduction (8, 17, 45, 57). It is hypothesized that rodents increase their activity due to an increased drive to forage for food, as the elevated activity is decreased when food is made available (36). The differential regulation of physical activity in response to calorie reduction has been hypothesized to be dependent on whether an animal has a sufficient amount of stored energy to make it through a time of famine metabolizing stored energy (slowing activity would protect their energy stores) or whether their stored energy is low and thus survival would be dependent on finding food and increasing activity would facilitate foraging (52, 53). A study in emperor penguins provides further support for this hypothesis, as the
penguins decrease their activity in response to the first three months of fasting, but when their
energy stores become depleted their activity begins to increase (56).

A potential concern of using accelerometers mounted on collars to measure physical
activity is the accuracy with which they detect whole body movement. To address this we
conducted a validation study in which we simultaneously measured physical activity by
accelerometers mounted on collars and videotaped 16 monkeys (51). Frame by frame analysis
was used to determine which behaviors generated activity counts and we found that activity
counts were strongly associated with whole body movement but, not head, neck or limb
movement (51). More recently we have used accelerometer-derived data to assess sleep and
looked at the minute-by-minute data and found the monkeys sit for longer periods of time than
humans and that there are long stretches in the night and day in which zero activity counts are
detected. Based on these studies we believe that collar-worn accelerometers are an excellent
way to accurately assess physical activity in nonhuman primates. It is also important to note
that the monkeys used in Experiment 1 were individually housed. Interestingly, we find that the
activity level of an individual animal is similar in individual cages and group housing (65), thus
we feel that the findings in this experiment are also applicable to individuals with access to a
larger housing environment.

Two studies have reported that exercise can prevent a diet-induced decrease in energy
expenditure (20, 47). In contrast, two other studies comparing weight loss in individuals that
either dieted or dieted and exercised report similar weight loss (27) or greater weight loss in the
group that only dieted (4). The studies showing an exercise-induced prevention of diet-induced
energy expenditure documented participation in an exercise program, but did not directly
measure daily level of physical activity and so did not examine whether participating in
purposeful exercise for a part of the day would change physical activity level during the
remaining portion of the day. To address this directly, in the current study a second group of 3
monkeys ran on a treadmill for 1 hr/day, 5 days/week. We found this led to a $6.1 \pm 1.2$ percent
weight loss and a calculated increase in calorie expenditure of 69.6±10.7 kcal/day (equivalent to 49 kcal/day for 7 days), and after a 3 month period. Importantly, exercising did not change the amount of physical activity during the other 23 hours of the day. This finding suggests that combining exercise with dieting will promote weight loss by compensating for the diet-induced decrease in energy expenditure. However, this conclusion is based on a calculation and it would be worthwhile for future studies to directly test this hypothesis by measuring exercise-associated energy expenditure during dieting. In humans, running an hour a day five times a week expends between 700 (for the average woman) and 860 (for the average man) extra calories per day (2). As in monkeys, this expenditure would similarly compensate for the decrease in physical activity in response to dieting [167 kcals/day x 5 days/week = 835 kcal (74)], and would thereby enhance diet-induced weight loss. In addition to participating in planned exercise regimens, recent studies indicate that it is possible to effectively increase daily physical activity by making small lifestyle changes, such as playing activity-promoting video games instead of traditional video games (39), and standing instead of sitting at desks while at school or work (40).

In this study, we found that dieting decreased both fat mass and lean tissue mass, but did not change overall percent body fat. Similar results have been reported in several human studies which find that caloric restriction reduces both fat and lean tissue mass (48, 76). In contrast, other studies report that the majority of weight loss with a low calorie diet is fat mass (75%) (3, 6). The loss in lean tissue with dieting is concerning and dieting has also been reported to decrease muscle tissue mass, strength and aerobic capacity (76). In contrast, weight loss occurring with exercise has been shown to not decrease lean tissue mass (67) and to actually improve strength and muscle mass (76). Thus, combining exercise with dieting is important in maintaining physical fitness and preserving muscle mass while still reducing body fat mass.
It is important to note that the monkeys in this study were ovariectomized females, an animal model of post-menopausal women. Several studies find that the body weight and fat responses to the initiation of exercise training and to energy deficit are gender-dependent (16, 24), thus the results of this study are most applicable to post-menopausal women and caution should be used in extending the findings to pre-menopausal females and males. Future studies are needed which objectively measure activity in pre-menopausal females and males during diet-induced weight loss.

We conclude that decreased physical activity is the primary mechanism the body uses to defend against diet-induced weight loss, and an exercise program of five hours of running per week is sufficient to prevent the diet-induced decrease in activity. As losing weight and then maintaining weight loss is quite difficult for most people, the findings of this study argue that increased emphasis should be placed on preventing weight gain over adulthood. Our previous studies indicate that the amount of physical activity that an individual undertakes is the best predictor of adult weight gain (66), suggesting that development of obesity in adulthood could be best prevented by maintaining elevated levels of physical activity across the adult years. Thus, increased physical activity appears to be the most effective means of both preventing and treating adulthood obesity.
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References


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Figure Legends

**Figure 1.** (Panel A) Percent change in body weight during 4 weeks of 30% calorie restriction and 4 weeks of 60% calorie restriction. Weight for each monkey was normalized to its body weight at the beginning of the study (week 0). (Panel B) Percent change in activity measured by accelerometer during the periods of 30% and 60% calorie restriction, compared to week 0. Asterisks indicate a significant \(p<0.05\) change from baseline.

**Figure 2.** (Panel A) Total metabolic rate, measured across a 24-hour day in each monkey at baseline (solid bar) and at the end of the 8-week diet period (open bar). The mean decrease in metabolic rate from the beginning to end of the diet period was 68 kcal. (Panel B) Activity associated energy expenditure measured across a 24-hour day in each monkey at baseline (solid bar) and at the end of the 8-week diet period (open bar). The mean decrease in activity associated energy expenditure was 41 kcal. Asterisks indicate a significant \(p<0.05\) difference from baseline.

**Figure 3.** (Panel A) Mean activity measured across the 24-hour day by accelerometer in 3 monkeys at baseline before monkeys started running on the treadmill 5 days/week and mean activity during the 23 hours/day when monkeys were not running at the end of 12 weeks of running (mean activity shown by bars). (Panel B) Percent increase in total activity measured across the 24-hour day at the end of 12 weeks of running compared to the baseline period.
Table 1: Body Composition (Mean ± SEM). Asterisks indicate a significant difference from baseline measures.

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<td>Percent Lean tissue</td>
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Figure 1. (Panel A) Percent change in body weight during 4 weeks of 30% calorie restriction and 4 weeks of 60% calorie restriction. Weight for each monkey was normalized to its body weight at the beginning of the study (week 0). (Panel B) Percent change in activity measured by accelerometer during the periods of 30% and 60% calorie restriction, compared to week 0. Asterisks indicate a significant ($p < 0.05$) change from baseline.
Figure 2. (Panel A) Total metabolic rate, measured across a 24-hour day in each monkey at baseline (solid bar) and at the end of the 8-week diet period (open bar). The mean decrease in metabolic rate from the beginning to end of the diet period was 68 kcal. (Panel B) Activity associated energy expenditure measured across a 24-hour day in each monkey at baseline (solid bar) and at the end of the 8-week diet period (open bar). The mean decrease in activity associated energy expenditure was 41 kcal. Asterisks indicate a significant (p<0.05) difference from baseline.
Figure 3. (Panel A) Mean activity measured across the 24-hour day by accelerometer in 3 monkeys at baseline before monkeys started running on the treadmill 5 days/week and mean activity during the 23 hours/day when monkeys were not running at the end of 12 weeks of running (mean activity shown by bars). (Panel B) Percent increase in total activity measured across the 24-hour day at the end of 12 weeks of running compared to the baseline period.