Improvements in Body Composition, Glucose Tolerance, and Insulin Action Induced by Increasing Energy Expenditure or Decreasing Energy Intake\textsuperscript{1,2}

Edward P. Weiss\textsuperscript{3} and John O. Holloszy\textsuperscript{*}

Division of Geriatrics and Nutritional Sciences, Department of Internal Medicine, Washington University School of Medicine, St. Louis, MO 63110

Abstract

Increases in exercise energy expenditure without compensatory changes in food intake (EX) and restriction of calorie intake (CR) both decrease body weight and fat mass, which, in turn, improve glucoregulatory function. However, EX may provide greater benefits than can be provided through CR. Therefore, our study hypothesis was that weight loss through EX reduces visceral abdominal fat and improves glucoregulation to a greater extent than does similar weight loss through CR. Forty-eight sedentary 50- to 60-y-old men and women, most of whom were overweight, underwent 12 mo of EX, CR, or a healthy lifestyle control period. Body composition was assessed by dual-energy x-ray absorptiometry and by magnetic resonance imaging. Indices of glucoregulatory function were determined by oral glucose tolerance test and were measured \textgreek{d}48 h after the last exercise bout in the EX group. Body weight, total fat mass, and visceral fat volume decreased similarly in the EX and CR groups but did not change in the HL group. Likewise, insulin sensitivity index and the oral glucose tolerance test glucose and insulin areas under the curve improved similarly in the EX and CR groups and remained unchanged in the HL group. In conclusion, weight losses induced by exercise and by CR are effective means for improving glucose tolerance and insulin action in nonobese, healthy, middle-aged men and women; however, it does not appear that exercise training-induced weight loss results in greater improvements than those that result from CR. J. Nutr. 137: 1087–1090, 2007.

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\textsuperscript{3}Present address: Department of Nutrition and Dietetics, St. Louis University, St. Louis, MO 63104.

\textsuperscript{4}Abbreviations used: CR, calorie restriction intervention; DEXA, dual X-ray absorptiometry; DLW, doubly labeled water; EX, exercise intervention; FFA, free fatty acid; HL, healthy lifestyle control intervention; ISI, insulin sensitivity index; OGTT, oral glucose tolerance test; SAT, abdominal subcutaneous adipose tissue volume; TEE, total energy expenditure; TNF-\textgreek{a}, tumor necrosis factor-\textgreek{a}; VAT, abdominal visceral adipose tissue volume.

\textsuperscript{6}To whom correspondence should be addressed. E-mail: jhollosz@im.wustl.edu.

Introduction

Calorie restriction (CR)\textsuperscript{4} slows the aging process and increases maximal lifespan in various short-lived organisms (1) and has numerous physiologic benefits in nonhuman primates (2,3). However, little is known regarding the effects of long-term CR with good nutrition in nonobese humans. Feasibility studies for human CR, referred to as CALERIE (Comprehensive Assessment of Long-term Effect of Reducing Intake of Energy), were completed recently at Tufts University (Boston, MA; Principal Investigator, Susan B. Roberts), the Pennington Biomedical Research Center (Baton Rouge, LA; Principal Investigator, Eric Ravussin), and at Washington University School of Medicine (St. Louis, MO; Principal Investigator, John O. Holloszy). At the Washington University site for CALERIE phase 1, we compared the effects of 20% CR with those of a 20% increase in energy expenditure induced by exercise with caloric intake kept constant (EX). Reductions in body weight and abdominal fat, induced by CR or by EX, improve insulin action and glucose tolerance (4), which are often impaired in overweight and obese individuals (5,6). In addition to weight loss induced by an energy deficit, exercise induces increases in muscle insulin sensitivity and responsiveness that are independent of weight loss (7).
Exercise training intervention. The exercise training intervention was designed to induce a 16% energy deficit during the first 3 mo and a 20% deficit during the remaining 9 mo by holding energy intake constant at baseline levels and increasing exercise energy expenditure. Exercise energy expenditure goals were given to the participants during weekly meetings with exercise trainers. The participants exercised, either in our facility or on their own, while using wrist watch-type HR monitors (S610, Polar Electro Oy), which stored exercise-specific data for energy expenditure.

Calorie restriction intervention. The objective of the CR intervention was to induce the same energy deficit as was prescribed for the EX group but by restricting energy intake. The intervention was administered by study dietitians who met with the participants on a weekly basis and educated the participants on practical aspects of reducing energy intake.

Healthy lifestyle intervention. Participants in the HL control group were offered advice for eating a healthy diet and were offered free access to off-site yoga classes but did not receive instructions to change either exercise or diet behaviors. Few of the subjects in the HL group took advantage of the offered services.

Body composition. Total and truncal fat mass and total fat-free mass were measured by dual-energy x-ray absorptiometry (DEXA; Delphi W, Hologic, software version 11.2) using the manufacturer’s recommendations. Abdominal fat mass, defined as the region between thoracic vertebra 12 and the inferior end of the sacroiliac joint, was also measured by DEXA. Visceral and subcutaneous adipose tissue volumes (VAT and SAT, respectively) were measured by MRI (Siemens) and subsequent computer analysis of images (HIPPO, version 1.3) (15). The superior end of the 10-cm longitudinal region of interest corresponded to the first lumbar vertebra, which was identified by locating the origin of the psoas muscle.

Energy intake. Energy intake was measured at baseline and 1, 3, 6, 9, and 12 mo using the doubly labeled water method (DLW) and 7-d food diaries. At baseline, the DLW-based estimates of energy intake were calculated as the average of 2 2-wk assessments of total energy expenditure (TEE); energy intake was assumed to equal TEE because the participants were weight stable. For each of the follow-up assessments, energy intake was based on a single 2-wk DLW assessment, and energy intake was calculated as TEE with adjustments for changes in total body energy stores as estimated from changes in DEXA-measured fat mass and fat-free mass. Self-reported energy intake was estimated using 7-d food diaries and computerized nutrient analysis (Nutrition Data System for Research, versions 4.05, 4.06, and 5.0; Nutrition Coordinating Center, University of Minnesota, Minneapolis MN).

Oral glucose tolerance, insulin action, and fasting glucoregulatory factors. Two-hour, 75-g oral glucose tolerance tests (OGTT) were performed according to the recommendations of the American Diabetes Association (16) with blood sampling for plasma glucose and insulin concentrations every 30 min during the test. All participants were instructed to refrain from exercise for at least 48 h before each OGTT. An estimate of whole-body insulin action (ISI) was calculated from the OGTT glucose and insulin data according to Matsuda and DeFronzo (17), and the glucose and insulin areas under the curve from the OGTT were calculated using the trapezoidal rule. Fasting blood was assessed for concentrations of free fatty acids (FFA), adiponectin, and tumor necrosis factor-α (TNF-α) using commercially available assay kits.
CR was just as effective as exercise for improving glucose tolerance and insulin action. Although it is well documented that fat loss results in improvements in glucose tolerance in overweight individuals, the mechanisms involved are still controversial. One hypothesis relates to plasma FFA concentrations, which have been reported to be higher in insulin-resistant overweight and obese individuals. In the present study, both the EX- and CR-induced weight losses resulted in reductions in fasting FFA concentrations. However, these decreases were small (EX, initial $= 646 \pm 210$, final $= 586 \pm 254 \text{ mmol/L, } P < 0.05$; CR, initial $= 569 \pm 231$, final $= 501 \pm 203 \text{ mmol/L, } P < 0.05$) and not statistically significant. It also seems unlikely that these small changes could have played a major role in the improvement in insulin action. Another hypothesis is that the improvement in insulin action is mediated by production of larger amounts of insulin sensitizing agents and decreased production of insulin resistance-causing agents by the smaller fat cells after weight loss. In the present study, and as shown in Fig. 5, increases in adiponectin, which are thought to improve insulin action, and decreases in TNF-$\alpha$, an insulin resistance factor, were both relatively small. However, both EX and CR resulted in significantly lower values for the ratio of TNF-$\alpha$ to adiponectin than occurred in the control group. A decrease in this ratio appears to be associated with improved insulin action (18).

It was our hypothesis that exercise would be more effective in improving insulin action than caloric restriction that results in similar fat loss because of the insulin sensitizing effects of exercise that occur in the absence of weight loss. The results of this study provide evidence that negative energy balances induced by calorie restriction or exercise are similarly effective in inducing fat loss and improved glucose tolerance and insulin action. A possible explanation for this finding is that the insulin

Figure 1 Fat mass in the trunk (A) and in the abdomen (B) in humans undergoing CR, EX, or HL interventions as measured by DEXA. Data are arithmetic means ± SEM. *$P < 0.05$ vs. baseline within group by paired $t$ test. $^{1}P \leq 0.05$ vs. HL group by ANCOVA and Tukey tests after adjustment for baseline values. EX, exercise training group; CR, calorie restriction group; HL, healthy lifestyle control group.

Figure 2 Fat volume in the visceral abdominal (A) and in the subcutaneous abdominal (B) compartments in humans undergoing CR, EX, or HL intervention as measured by MRI. Data are arithmetic means ± SEM. *$P < 0.05$ vs. baseline within group by paired $t$ test. $^{1}P \leq 0.05$ vs. HL group by ANCOVA and Tukey tests after adjustment for baseline values, age, and sex.

Figure 3 Energy intake in humans undergoing CR, EX, or HL intervention as determined by DLW with adjustments for changes in total energy stores by DXA (DLW/DXA, A) and by food diary (B). Data are arithmetic means ± SEM. *$P < 0.05$ vs. baseline within group by paired $t$ test. $^{1}P < 0.05$ vs. EX and HL groups by ANCOVA and Tukey tests after adjustment for baseline values.

Figure 4 Changes in OGTT-based outcomes in response to EX, CR, and HL interventions in humans. ISI was calculated according to Matsuda and DeFronzo (17). *$P < 0.05$ for within group change by paired $t$ test. $^{1}P < 0.05$ vs. HL group by ANCOVA and Tukey tests after adjustment for baseline values. ISI and the AUC for insulin were log transformed for statistical analyses. Although insulin AUC means do not appear to differ between the CR and HL groups, these means were statistically different after adjustment for differences in baseline insulin AUC values among groups.
sensitizing effects of exercise are short term and had probably worn off by the time that we made our measurements. It seems likely that the improvements in insulin action were mediated by the reductions in body fat mass, which were similar in the 2 groups.

Literature Cited


