Effects of an intensive short-term diet and exercise intervention: comparison between normal-weight and obese children

Christian K. Roberts,1 Ali Izadpanah,1,2 Siddhartha S. Angadi,1 and R. James Barnard2

1Exercise and Metabolic Disease Laboratory, Translational Section, School of Nursing, University of California Los Angeles, Los Angeles, California; and 2Department of Integrative Biology and Physiology, University of California Los Angeles, Los Angeles, California

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Roberts CK, Izadpanah A, Angadi SS, Barnard RJ. Effects of an intensive short-term diet and exercise intervention: comparison between normal-weight (N) and obese (O) children. Am J Physiol Regul Integr Comp Physiol 305: R552–R557, 2013. First published July 24, 2013; doi:10.1152/ajpregu.00131.2013.—Lifestyle intervention programs currently emphasize weight loss secondary to obesity as the primary determinant of phenotypic changes. We examined whether the effects of a short-term lifestyle intervention program differ in normal-weight versus overweight/obese children. Nineteen overweight/obese (O; BMI = 33.6 ± 1.9 kg/m2) and 14 normal-weight (N; BMI = 19.9 ± 1.5 kg/m2) children participated in a 2-wk program consisting of an ad libitum high-fiber, low-fat diet and daily exercise (2–2.5 h). Fasting serum samples were taken pre- and postintervention for determination of lipids, glucose homeostasis, inflammatory cytokines, and adipokines. Only the O group lost weight (3.9%) but remained overweight/obese (32.3 ± 1.9 kg/m2). Both groups exhibited significant intervention-induced decreases (P < 0.05) in serum insulin (N: 52.5% vs. O: 28.1%; between groups, P = 0.38), homeostatic model assessment for insulin resistance (N: 53.1% vs. O: 28.4%, P = 0.43), leptin (N: 69.3% vs. O: 44.1%, P = 0.10), amylin (N: 28.7% vs. O: 26.1%, P = 0.80), resistin (N: 40.6% vs. O: 35.1%, P = 0.99), plasminogen activator-inhibitor-1 (N: 30.8% vs. O: 25.6%, P = 0.59), IL-6 (N: 58.8% vs. O: 41.6%, P = 0.08), IL-8 (N: 46.0% vs. O: 42.2%, P = 0.49), and TNFα (N: 45.8% vs. O: 40.8%, P = 0.99). No associations between indices of weight change and phenotypic changes were noted. A short-term, intensive lifestyle modification program is effective in ameliorating metabolic risk factors in N and O children. These findings suggested that lifestyle changes may be the underlying drivers of changes in metabolic and cardiovascular phenotypes. This led us to test the validity of overweight/obesity status as a primary cause of metabolic abnormalities by investigating the effects of an identical lifestyle intervention in normal-weight compared with overweight/obese children. Thus, the present study was designed to examine the efficacy of a short-term daily exercise and plant-based ad libitum diet intervention program on serum endocrine and cytokine markers. We examined its effects on interleukin (IL)-8, IL-10, IL-1 receptor antagonist (IL-1ra), IL-6, tumor necrosis factor-α (TNFα), plasminogen activator-inhibitor (PAI)-1, resistin, amylin, and leptin in normal weight versus obese children. We hypothesized that normal-weight and obese children would respond similarly to the lifestyle intervention program irrespective of baseline obesity status, suggesting that dietary intake and lack of exercise/physical activity are the underlying causes of the phenotypic abnormalities noted.

METHODS

Subjects. Normal-weight and overweight/obese children [classified by the Centers for Disease Control (CDC) as sex-specific BMI-for-age percentiles] participated voluntarily in the Pritikin Longevity Center 2-wk residential lifestyle modification program, where a plant-based diet was provided ad libitum and daily exercise (2–2.5 h) performed. Pre- and postintervention data were obtained from 19 overweight (O) children aged 8–17 yr (mean 13.1 ± 0.5 yr, 9 males and 10 females; mean BMI: 33.6 ± 1.9 kg/m2; BMI percentile: 95.2 ± 1.4%) and 14 normal-weight (N) children aged 9–15 yr (mean 11.2 ± 0.5 yr, 6 males and 8 females, 19.9 ± 1.5 kg/m2, 55.5 ± 7.9%) who participated in the 2-wk program. All subjects in the O group had a BMI >85th percentile, and 13 of the 19 were >95th percentile (obese) according to CDC BMI-for-age percentile standards. All 14 subjects in the N group were considered to be at a healthy weight (>5th and

Address for reprint requests and other correspondence: C. K. Roberts, Exercise and Metabolic Disease Laboratory, Translational Sciences Section, UCLA School of Nursing 700 Tiverton Ave., Los Angeles, CA 90095-6918 (e-mail: croberts@ucla.edu).
Anthropometric and metabolic phenotypes in normal-weight and obese children

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Obese Subjects (n = 19)</th>
<th>Normal-Weight Subjects (n = 14)</th>
<th>%Change</th>
<th>%Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight, kg</td>
<td>94.0 ± 7.4</td>
<td>90.3 ± 7.1</td>
<td>−3.9‡</td>
<td>−2.3</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>33.6 ± 1.9</td>
<td>32.3 ± 3.8</td>
<td>−3.8§</td>
<td>−2.3*</td>
</tr>
<tr>
<td>WC, cm</td>
<td>97.2 ± 5.7</td>
<td>93.0 ± 4.8</td>
<td>−4.3‡</td>
<td>−4.8</td>
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<tr>
<td>RHR</td>
<td>95 ± 4</td>
<td>80 ± 3</td>
<td>−15.4</td>
<td>−7.8</td>
</tr>
<tr>
<td>SBP</td>
<td>125 ± 4</td>
<td>115 ± 2</td>
<td>−8.1‡</td>
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<tr>
<td>DBP</td>
<td>73 ± 3</td>
<td>68 ± 2</td>
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<td>−7.6</td>
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<tr>
<td>Glucose, mg/dl</td>
<td>813 ± 2.0</td>
<td>858 ± 1.3</td>
<td>5.5</td>
<td>−1.3</td>
</tr>
<tr>
<td>Insulin, μU/ml</td>
<td>223 ± 3.5</td>
<td>161 ± 4.2</td>
<td>−28.1*</td>
<td>−52.5‡</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>4.8 ± 0.8</td>
<td>3.4 ± 0.8</td>
<td>−28.4*</td>
<td>−53.1‡</td>
</tr>
<tr>
<td>QUICKI</td>
<td>0.31 ± 0.01</td>
<td>0.33 ± 0.01</td>
<td>4.9‡</td>
<td>9.3‡</td>
</tr>
<tr>
<td>TG, mg/dl</td>
<td>157.7 ± 14.7</td>
<td>86.0 ± 7.9</td>
<td>−37.5‡</td>
<td>−41.1‡</td>
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<tr>
<td>Total cholesterol, mg/dl</td>
<td>166 ± 6.2</td>
<td>132.0 ± 5.8</td>
<td>−20.8§</td>
<td>−23.3</td>
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<tr>
<td>LDL cholesterol, mg/dl</td>
<td>95.0 ± 3.1</td>
<td>71.8 ± 5.0</td>
<td>−24.8%</td>
<td>−29.4%</td>
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<tr>
<td>HDL cholesterol, mg/dl</td>
<td>44.0 ± 2.2</td>
<td>43.1 ± 2.7</td>
<td>−2.1</td>
<td>−5.0</td>
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<tr>
<td>Total/HDL cholesterol</td>
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<td>−18.2‡</td>
<td>−19.0‡</td>
</tr>
<tr>
<td>LDL/HDL</td>
<td>2.3 ± 0.2</td>
<td>1.8 ± 0.2</td>
<td>−20.7†</td>
<td>−24.0‡</td>
</tr>
</tbody>
</table>

All data are expressed as means ± SE. Pre, preintervention; post, postintervention; WC, waist circumference; RHR, resting heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; HOMA-IR, homeostatic model assessment for insulin resistance; QUICKI, quantitative insulin sensitivity check index; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein. Anthropometric and lipid measurements in normal-weight and obese children undergoing a 14-day diet and exercise intervention. †P < 0.01, baseline differences between the normal-weight and obese groups;‡P < 0.01; *P < 0.05.
0.10) had comparable decreases in both groups but only significantly in the O group (N: DBP $P = 0.09$, SBP $P = 0.8$, RHR $P = 0.082$).

Total cholesterol (N: 23.3% vs. O: 20.8%, $P = 0.84$), LDL (N: 29.4% vs. O: 24.5%, $P = 0.81$), and TG (N: 41.1% vs. O: 37.5%, $P = 0.63$) all had similar significant decreases in both groups ($P < 0.01$). Serum HDL (N: 5.0% vs. O: 2.1%, $P = 0.38$) decreased nonsignificantly in both N ($P = 0.07$) and O ($P = 0.44$).

Insulin (N: 52.5% vs. O: 28.1%, $P = 0.38$) decreased in both groups, whereas glucose did not change significantly in N (1.3% decrease, $P = 0.66$) or O (5.5% increase, $P = 0.05$), nor was there a difference between the N and O ($P = 0.10$). However, HOMA-IR (N: 53.1% vs. O: 28.4%, $P = 0.43$) had similar significant decreases in both groups ($P < 0.05$), and QUICKI (N: 9.3% vs. O: 4.9%, $P = 0.12$) increased significantly in both groups ($P < 0.01$), which was driven mainly by the decrease in insulin.

Cytokines, adipokines, and endocrine markers. All biomarkers were similar at baseline between the two groups, except for PAI-1 ($P < 0.01$), leptin ($P < 0.001$), and IL-1ra ($P < 0.05$) (Figs. 1, 2, and 3). Serum PAI-1 (N: 30.8% vs. O: 25.6%, $P = 0.59$), resistin (N: 40.0% vs. O: 35.1%, $P = 0.99$), amylin (N: 28.7% vs. O: 26.1%, $P = 0.80$), and leptin (N: 69.3% vs. O: 44.1%, $P = 0.10$) decreased significantly ($P < 0.01$) and similarly in both groups. Adiponectin (N: 29.3% vs. O: 41.8%, $P = 0.78$) increased in both groups but was only statistically significant in O ($P < 0.01$; N: $P = 0.12$).

Cytokine changes also exhibited similar responses between the N and O groups. IL-6 (N: 58.8% vs. O: 48.5%, $P = 0.78$), IL-8 (N: 46.0% vs. O: 42.2%, $P = 0.49$), and TNFα (N: 45.8% vs. O: 40.8%, $P = 0.99$) decreased significantly in both groups ($P < 0.05$). IL-1ra decreased nonsignificantly in both groups (N: 32.8% vs. O: 19.9%, $P = 0.90$). IL-10 did not change in either group (N: 7.0% decrease vs. O: 4.9% increase, $P = 0.77$).

Additionally, we did not detect any significant correlations between changes in waist circumference, body weight, or BMI with changes serum cytokines, adipokines, or endocrine markers (all $r$ values ranged between −0.34 and 0.41, all $P > 0.12$).

**DISCUSSION**

Currently, there is the perception that obesity is causally implicated in the pathogenesis of dyslipidemia, insulin resistance, inflammation, and other features related to metabolic health. It is certainly the case that adipose tissue, depending on location and characteristics, may exacerbate various risk factors. For example, it is well-established that visceral fat contributes to worsening of metabolic health (6, 25). However, if obesity is the primary cause, then 1) reversal of obesity would be required to reverse phenotypic abnormalities, and 2) subjects who were not obese would not respond similarly to obese subjects. Regarding the first point, in previous seminal studies, we demonstrated that short-term lifestyle modification could ameliorate metabolic syndrome phenotypes in both men (19) and children (10). In addition, a variety of cardiovascular disease risk factors were improved in men (19, 20), women (28), and children (4, 18) despite modest weight loss and subjects remaining overweight/obese by BMI classification. Furthermore, when we correlated changes in body weight or BMI with changes in phenotypic outcomes, no signifi-

![Fig. 1](http://ajpregu.physiology.org/Downloadedfrom) Effect of diet and exercise intervention on serum concentration of the cytokines IL-8, IL-6, TNFα, IL-10, and IL-1 receptor antagonist (IL-1ra) in normal-weight (filled bars) and obese children (open bars). All data are expressed as means ± SE. †$P < 0.01$ and *$P < 0.05$, postintervention (post) vs. preintervention (pre). ‡$P < 0.05$, baseline differences between the normal-weight and obese groups. The baseline difference between normal-weight and obese group for IL-10 was $P = 0.12$. 

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significant associations were noted. However, we did find significant correlations between various fatty acid species and inflammatory factors (10).

Regarding the second point, the present study was designed to test the hypothesis that responsiveness to a short-term daily physical activity and plant-based ad libitum diet intervention program would be similar between normal-weight and overweight/obese children. An advantage of using a short-term intervention is that lifestyle changes can be assessed independently of obesity reversal. The findings of the current study indicated that effects were similar in both overweight/obese and normal-weight subjects. This occurred even for metabolic outcomes that exhibited significant differences at baseline (PAI-1, leptin, and IL-1ra). Furthermore, the normal-weight

![Graphs showing changes in metabolic markers](http://ajpregu.physiology.org/)

**Fig. 2.** Effect of diet and exercise intervention on serum concentration of the metabolic risk markers plasminogen activator-inhibitor-1 (PAI-1), resistin, adiponectin (ACRP), leptin, and amylin in normal-weight (filled bars) and obese (open bars) children. All data are expressed as means ± SE. ‡P < 0.01, post-vs. preintervention; †P < 0.05, baseline differences between the normal-weight and obese groups.

![Graphs showing changes in cytokine markers](http://ajpregu.physiology.org/)

**Fig. 3.** Effect of diet and exercise intervention on %changes in concentration of cytokines and metabolic risk markers in normal-weight and obese children. No differences in changes between normal-weight and obese groups were noted post- vs. preintervention. %Changes from baseline were calculated based on the geometric mean. All data are expressed as means. Error bars represent the 95% confidence interval.
subjects had responses in measured phenotypes/metabolic markers that were similar to the overweight/obese subjects despite not being overweight/obese at baseline or exhibiting weight loss. The potential contributing lifestyle factors involved in the changes seen in the metabolic profile have been discussed previously (10) and likely include the decrease in saturated fats and refined sugar consumption, the increase in ω-3 fatty acids and nutrients (vitamins, minerals, phytochemicals, and fiber) from the diet, and the increase in physical activity, all of which can alter inflammatory and oxidative processes. Interestingly, the changes in serum cytokines, adipokines, and endocrine markers were not associated with changes in body weight, BMI, or waist circumference in either group. One explanation for the similar effect is that both the normal-weight and obese subjects improve phenotypes related to lipid levels, insulin resistance, and adipokines, etc., but the obese subjects have a genetic predisposition (1) to gain weight more readily compared with normal-weight subjects. It is known that many obese subjects are not metabolically unhealthy (24), whereas many normal-weight individuals (by BMI) are metabolically unhealthy (29). Thus, long-term, it is possible that with continued lifestyle modification obesity may be reversed, but even if not, a metabolically healthy obese phenotype can develop, as was noted in the short term with the obese subjects enrolled in the current study. Furthermore, given that weight loss attempts are typically associated with a high degree of recidivism in adult and pediatric populations (5, 8), lifestyle modification that focuses on the normalization of metabolic phenotypes may be of significant value in the pediatric population.

The noted benefits on metabolic, cardiovascular, and inflammatory biomarkers independent of weight loss are not surprising, and it is apparent that the relationships between body weight and lifestyle are complex. For example, Phillips et al. (15) and Varady et al. (27) provided different diets to obese young adults and noted that, despite both groups exhibiting significant weight loss and decreased blood pressure, a “low-fat” diet improved whereas a “low-carbohydrate” diet worsened endothelial function. In addition, Bradley et al. (3) noted that a low-fat diet improved whereas a low-carbohydrate diet worsened augmentation index. Krogh-Madsen et al. (11) and Olsen et al. (14) noted that with a short-term decrease in daily physical activity there was decreased insulin sensitivity and aerobic fitness despite modest weight loss. Interestingly, in the Diabetes Prevention Program, those who met only the physical activity goal and not the weight loss goal had a 44% decrease in diabetes incidence (9), whereas in the Finnish Diabetes Trial, achieving 4 h/wk of physical activity led to a reduction in diabetes risk in subjects who did not lose weight (26).

Also of interest in our cohort is the fact that baseline and percent change in several of the biomarkers were similar in normal-weight and obese children, suggesting similar cardiovascular disease risk profiles. The Pathobiological Determinants of Atherosclerosis in Youth study demonstrated coronary atherosclerosis in both normal-weight and obese males, but it was more severe in the obese males (12). It is possible that the mechanisms by which normal-weight and obese subjects improve in an intervention of this type differ; however, this would require further investigation, using molecular techniques to establish potential differences.

The current study has important strengths and limitations to consider. The major strength of the study is the monitoring permitted by the study. Monitoring food intake and physical activity reduces the need to query subjects about their compliance or to rely on food and activity questionnaires. Furthermore, all exercise sessions were supervised, facilitating adherence to the diet and activities. Additionally, the diet was ad libitum, a major advantage in cases where overeating is an issue, and thus, this is a more realistic program to implement into the daily lives of children rather than intentional caloric restriction. A limitation of the present study is the lack of body composition data to determine the fat mass and lean mass of both groups. Additionally, we did not look at diet and exercise independently, and therefore, we cannot attribute the changes directly to either aspect of the intervention.

Overall, short-term intensive lifestyle modification is effective in ameliorating several metabolic risk factors similarly in both normal-weight and overweight/obese children. Furthermore, because the normal-weight children were not obese and we did not find any associations between changes in indices of obesity and our serum measurements, baseline obesity and weight loss per se were not the primary drivers leading to the phenotypic changes noted. These findings suggest that dietary intake and exercise/physical activity changes may be the underlying causes of the phenotypic changes noted. Additionally, the normal-weight subjects exhibited metabolic abnormalities that were likely due to their ongoing diet and lifestyle habits. Even though current public health recommendations are centered on overweight/obesity and the metabolic abnormalities associated with the same, we have demonstrated that there may be room for improvement in the metabolic profiles of individuals who are not overweight/obese. Given that body weight and weight change are poor surrogates for lifestyle (2), these findings reinforce the need to remind even normal-weight individuals about healthy lifestyle choices. Furthermore, therapies driven by BMI classification and weight loss in young patients may lead to missed opportunities to counsel them on the benefits of weight loss-independent effects of lifestyle modification, including proper diet and physical activity (21, 22). Overall, the results support the need for larger, randomized, long-term studies to investigate the impact of lifestyle modification on disease outcomes independent of weight loss.

GRANTS

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DISCLOSURES

R.J. Barnard received a consulting honorarium from the Pritikin Longevity Center.

AUTHOR CONTRIBUTIONS

C.K.R., A.I., and R.J.B. contributed to the conception and design of the research; C.K.R., A.I., and R.J.B. interpreted the results of the experiments; C.K.R. and A.I. drafted the manuscript; C.K.R., A.I., S.S.A., and R.J.B. edited and revised the manuscript; C.K.R., A.I., S.S.A., and R.J.B. approved the final version of the manuscript; A.I. performed the experiments; A.I. analyzed the data; A.I. prepared the figures.
REFERENCES


