

Effect of a Successful Intensive Lifestyle Program on Insulin Sensitivity and Glucose Tolerance in Obese Youth

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OBJECTIVE — To evaluate the impact on glucose metabolism of a lifestyle program (the Yale Bright Bodies Program) for obese children.

RESEARCH DESIGN AND METHODS — Thirteen Bright Bodies and ten clinic-care control subjects who were part of a large randomized clinical trial had 75-g oral glucose tolerance tests at the beginning and end of the 12-month study.

RESULTS — Bright Bodies subjects had significantly greater decreases in weight, BMI, and body fat than clinic-care subjects, and the Bright Body subjects' changes in body composition were accompanied by marked improvements in insulin sensitivity ($P = 0.009$) and glucose tolerance ($P = 0.04$).

CONCLUSIONS — An intensive lifestyle program that successfully reduces body weight and body fat can markedly improve insulin sensitivity and glucose metabolism in obese youth.

Diabetes Care 32:45–47, 2009

In an attempt to respond to the childhood obesity epidemic, we developed Yale's Bright Bodies weight-management program, a family-based lifestyle intervention that includes nutrition education, exercise, and behavior modification. Its efficacy was validated by a 12-month randomized clinical trial (RCT) with more than 170 overweight children and adolescents. In this RCT, Bright Bodies subjects had significant improvements in BMI and body composition, including a 9.2-kg difference in change in total body fat versus that in the clinic-care control group (1). To examine the impact of the Bright Bodies program on insulin sensitivity and glucose metabolism in obese children, a randomly selected subset of subjects from both groups underwent an oral glucose tolerance test (OGTT) at the beginning and end of the 12-month study.

RESEARCH DESIGN AND METHODS

The Bright Bodies RCT was approved by the Yale Human Investigation Committee. Written informed assent and consent were obtained from participants and parents. Subjects were recruited from the Yale Pediatric Obesity Clinic and had to have a BMI at or above the 95th percentile and be willing to participate in a weight-management program with a parent or caregiver for nutrition education (if randomized to the intervention group). Subjects were excluded if they had diabetes, were using a medication that affects weight or glucose metabolism, or had a medical condition that precluded program participation. Once randomized ~2:1 to either the intervention or control group, ~25% of subjects in each group were randomized to an OGTT (20 intervention and 14 control subjects) at baseline and 12 months. Thirteen intervention and 10 control subjects

completed both OGTTs. Baseline characteristics were similar to those of the general RCT and substudy, as were retention rates.

For the first 6 months, children exercised twice per week for 50 min and attended a nutrition or behavior-modification class for 40 min once per week. To mimic a maintenance phase, children attended the program every other week for the next 6 months. Control subjects were seen by Yale Pediatric Obesity Clinic staff every 6 months for follow-up evaluation and counseling. Physicians, nurse practitioners, and registered dietitians counseled children about improved nutrition and activity, and social workers offered brief psychosocial counseling. Control participants were offered eligibility to participate in the Bright Bodies program at the end of the study. More detailed methods have previously been described (1).

The day before an OGTT, subjects refrained from strenuous activity, consumed a >250 g carbohydrate diet, and fasted overnight. Height, weight, BMI, and body fat were measured using a stadiometer and Body Fat Analyzer (Tanita Corporation, Arlington Heights, IL). A catheter was inserted into an antecubital vein for blood sampling. After baseline samples were obtained for measurement of fasting plasma glucose and insulin, the subject drank a flavored glucose drink (Custom Laboratories, Baltimore, MD) containing 1.75 g/kg glucose to a maximum of 75 g. Blood for measurement of glucose and insulin was obtained at 0, 30, 60, 90, 120, and 180 min.

Plasma glucose was measured using a glucose analyzer (Beckman Instruments Inc., Fullerton, CA) and insulin by radioimmunoassay (Linco Laboratories, St. Charles, MO). Changes in insulin sensitivity were assessed by the whole body insulin sensitivity index derived from glucose and insulin levels during the OGTT (2). The areas under the curve (AUCs) for insulin (AUC_{insulin}) and glucose (AUC_{glucose}) were calculated using the trapezoidal rule (3). Group comparisons were made using paired Student's *t* tests,

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Received 12 May 2008 and accepted 26 September 2008.

Published ahead of print at <http://care.diabetesjournals.org> on 7 October 2008. DOI: 10.2337/dc08-0808.

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Table 1—Baseline characteristics and changes after 12 months in the Bright Bodies and control groups

	Baseline			Change after 12 months			P
	Bright Bodies	Control	P	Bright Bodies	Control	Treatment effect*	
n	13	10	—	13	10	—	—
IFG/IGT†	3 (23)	1 (10)	0.37	0 (0)	5 (50)	0.50 (0.09–0.80)‡	0.007*
Age (years)	11.3	12.1					
Sex (male)	4 (31)	5 (50)					
Race/ethnicity							
White	4 (31)	5 (50)					
Black	5 (38)	3 (30)					
Hispanic	4 (31)	2 (20)					
Height (cm)	150.79 ± 2.10	160.36 ± 3.41	0.256	4.02 ± 0.75	5.06 ± 0.63	−1.04 (−3.2 to 1.1)	0.323
Weight (kg)	78.78 ± 7.01	89.96 ± 5.99	0.836	4.18 ± 1.85	11.56 ± 1.12	−7.38 (−12.6 to −2.9)	0.031*
BMI (kg/m ²)	34.08 ± 2.29	34.70 ± 1.72	0.698	0.15 ± 0.67	2.15 ± 0.45	−2.00 (−4.0 to −0.4)	0.017*
BMI (z score)	2.40 ± 0.1	2.50 ± 0.08	0.387	−0.11 ± 0.06	0.06 ± 0.03	−0.17 (−0.3 to −0.01)	0.034*
Body fat (%)	45.95 ± 2.27	43.79 ± 2.52	0.101	−1.82 ± 1.4	7.17 ± 1.6	−8.99 (−13.6 to −4.3)	<0.001*
Lean body mass (kg)	42.42 ± 2.82	55.79 ± 3.35	0.755	4.62 ± 2.1	−1.24 ± 1.79	5.86 (−0.7 to 13.4)	0.076
Fat mass (kg)	35.53 ± 5.49	43.48 ± 3.13	0.023	−0.07 ± 1.26	13.05 ± 1.15	−13.12 (−17.1 to −9.2)	<0.001*
Fasting glucose (mg/dl)	91.8 ± 1.35	91.0 ± 2.33	0.734	−1.04 ± 0.89	2.6 ± 2.07	−3.64 (−7.9 to 0.7)	0.090
Glucose ₁₂₀ (mg/dl)	116.3 ± 5.73	113.3 ± 6.32	0.179	−5.54 ± 5.98	9.1 ± 5.82	−14.64 (−32.4 to 3.1)	0.100
AUC _{glucose} (mg/dl)	121.6 ± 4.81	121.9 ± 6.15	0.754	−5.38 ± 4.27	6.61 ± 2.98	−11.99 (−23.5 to 5.5)	0.042*
Fasting insulin (μU/ml)§	30.0 (9.7)	34.0 (19.2)	0.960	−4.5 (8.55)	3.0 (8.8)	−7.50 (−17.0 to 2.0)	0.070
AUC _{insulin} (μU/ml)§	147.1 (111.5)	102.1 (87.6)	0.290	−50.9 (84.57)	47.0 (63.9)	−97.9 (−161.5 to −34.3)	0.003*
WBISI§	1.51 (0.80)	2.42 (0.70)	0.500	0.63 (0.70)	−0.07 (0.58)	0.70 (0.04–1.56)	0.007*

Data are n, n (%), or means ± SEM of a paired *t* test unless otherwise indicated. *Treatment effect: difference in change in the Bright Bodies and control groups (95% CI). †P value based on Fisher's exact test. ‡Difference in proportions (95% CI) (ref. 7). §Wilcoxon's rank-sum test median (interquartile range) (ref. 8). IFG, impaired fasting glucose; IGT, impaired glucose tolerance; WBISI, whole body insulin sensitivity index.

Wilcoxon's rank-sum test, and Fisher's exact test where appropriate.

RESULTS— Except for the significantly greater total body fat mass (due to greater height) of control subjects ($P = 0.02$), there were no significant differences in baseline characteristics between the groups (Table 1). As previously reported for the RCT as a whole (1), control subjects who participated in the OGTT substudy had significant increases in weight ($P = 0.003$), BMI ($P = 0.017$), BMI z score ($P = 0.03$), and fat mass ($P < 0.001$) compared with the corresponding measures in intervention subjects (Table 1). The difference between the two groups with respect to change in total body fat was nearly twofold greater than the differences in change in body weight. Moreover, increase in weight in the intervention group was fully accounted for by increases in lean body mass.

Bright Bodies subjects had a 53% reduction in AUC_{insulin} and a 42% increase in whole body insulin sensitivity index, whereas the control subjects worsened in both parameters ($P = 0.0025$ and 0.007 , respectively). These improvements in insulin sensitivity were accompanied by a small but significantly greater decrease in

AUC_{glucose} in the intervention group than in the control group. It is noteworthy that fasting and 2-h plasma glucose levels normalized in all three intervention subjects with pre-diabetes (impaired glucose tolerance or impaired fasting glucose), whereas the number of pre-diabetic subjects in the control group increased from one to five ($P = 0.04$) after 12 months.

CONCLUSIONS— The aim of this study was to examine potential metabolic benefits of a lifestyle and exercise program for obese youth without diabetes. The most striking finding was that the Bright Bodies program resulted in marked improvements in insulin sensitivity and reductions in glucose-stimulated plasma insulin and glucose responses. These observations are important because insulin resistance and compensatory hyperinsulinemia have been suggested to be central pathophysiologic factors in other clinical and metabolic complications of obesity, even in children (4).

Because the changes in body weight and composition in the subjects randomly selected for this study were nearly identical in direction and magnitude to the changes of the intervention and control groups in the RCT as a whole, it is

reasonable to assume that the metabolic changes observed in this subset can be generalized to the larger group of subjects in the RCT.

The Diabetes Prevention Program demonstrated that an intensive lifestyle program for pre-diabetic adults that results in sustained weight loss can prevent or delay the development of type 2 diabetes (5). After the RCT, the reduced rate of weight gain and improvements in body composition seen in the growing children comprising the Bright Bodies group restored normal glucose metabolism in the three subjects with pre-diabetes at baseline, whereas the prevalence of pre-diabetes increased from 10 to 50% of subjects in the control group by the end of the study. This finding is of importance because obese pre-diabetic children who continue to gain excessive weight and body fat rapidly progress to type 2 diabetes (6).

Acknowledgments— This study was supported by grants from the National Institutes of Health (K24 HD001464 and R01 HD028016), the McPhee Foundation, and the Stephen I. Morse Pediatric Diabetes Research Fund and by CTSA Grant UL2

RR024139 from the National Center for Research Resources.

No potential conflicts of interest relevant to this study were reported.

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