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School-Based Intervention Acutely Improves Insulin Sensitivity and Decreases Inflammatory Markers and Body Fatness in Junior High School Students

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Context: Risk factors for type 2 diabetes mellitus (T2DM) include obesity, family history, dyslipidemia, a proinflammatory state, impaired insulin secretory capacity, and insulin resistance.

Objective: The aim of this study was to examine the effects of a 3- to 4-month school-based intervention consisting of health, nutrition, and exercise classes plus an aerobic exercise program on diabetes risk.

Design: This study was a randomized before/after controlled trial.

Methods: Seventy-three eighth-grade students in a predominantly Hispanic New York City public school were divided into a control group (studied twice without receiving the intervention) and an experimental group (studied before and after the intervention).

Outcome Measures: We measured body fatness (bioelectrical impedance), insulin sensitivity, β-cell function (insulin release in response to an iv glucose load corrected for insulin sensitivity), lipid profiles, and circulating concentrations of IL-6, C-reactive protein, adiponectin, and TNF-α.

Results: Participation in the intervention was associated with significant reductions in body fatness, insulin resistance, and circulating concentrations of C-reactive protein and IL-6, irrespective of somatotype on enrollment.

Conclusion: Short-term school-based health, nutrition, and exercise intervention is beneficial to all students and affects multiple diabetes risk factors. **(*J Clin Endocrinol Metab* 92: 504–508, 2007)**

TYPE 2 DIABETES mellitus (T2DM) is a complex metabolic disorder reflecting interactions among genes influencing diabetes susceptibility and an environment that favors the expression of that susceptibility by facilitation of obesity and a sedentary lifestyle (1). The percentage of new pediatric diabetic subjects who have type 2 has increased 10-fold over the past decade (2), and T2DM is now a pediatric disease whose incidence peaks in late puberty (2, 3). Aside from family history of disease, there are independent anatomic (body fatness) and biochemical (impaired insulin release, insulin resistance, dyslipidemia, and a proinflammatory state) risk factors for the development of T2DM.

Clinically, adiposity accounts for 55% of the variance in insulin sensitivity in children (3), and 80–90% of children and adults with T2DM are obese (2). Biochemically, impaired insulin release and insulin resistance convey, respectively, 2.4- and 2.1-fold increases in relative risk for progression to T2DM over a 4-yr period in nondiabetic adult subjects (4) and an elevated fasting insulin concentration is associated with a 5-fold increased risk of developing T2DM in euglycemic adult offspring of parents with T2DM (5). Even after risk adjustment for body mass index (BMI) and family history of T2DM, hypertriglyceridemia conveys a 1.4–4.5 increased T2DM risk over the ensuring 2–9 yr (6) in adults. Even adjusted for other risk factors, T2DM risk is increased 1.7-fold among adults in the lowest quartile for circulating concentrations of adiponectin (ACRP30) (7), and 4.2- and 2.3-fold, respectively, among those in the highest quartile for circulating concentrations of C-reactive protein (CRP) and IL-6 over a 4-yr period (8). Circulating concentrations of TNF-α are elevated in nondiabetic first-degree adult relatives of known type 2 diabetic subjects (9).

We prospectively assessed the effects of lifestyle intervention (exercise and health and nutrition education) on multiple risk factors for T2DM (insulin secretory capacity, insulin sensitivity, triglycerides, and circulating concentrations of inflammatory cytokines) in early adolescence.

Subjects and Methods

Subjects

Approval for these studies was obtained from the New York City school board, the New York City Board of Health, and the institutional review board of Columbia Presbyterian Medical Center and are consistent with guiding principles for research involving humans (10). Parental and student written informed consent or assent was obtained from 79 out of 136 students, of whom 73 completed the study. Failures to complete the study were due to transfer to another school (n = 2) or illness on testing dates (n = 4). Demographics of students who completed these studies were not significantly different from that of the class as a whole. All subjects represented the first or second generation of their family in the United States and identified themselves as having origins in the Dominican Republic except for one Liberian male. One class (n = 24) was randomly selected as a control group and did not receive the

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Abbreviations: AIR, Acute insulin response; BMI, body mass index; CRP, C-reactive protein; GDI, glucose disposal index; QUICKI, quantitative insulin sensitivity check index; T2DM, type 2 diabetes mellitus.

intervention until after students had been studied twice to assess progression of variables within the same time frame as subjects in the experimental group (n = 49).

Testing

At enrollment, family and medical history was ascertained from students and parents. Family history of T2DM was defined as a known affected first- or second-degree relative without assessment of whether other family members had undiagnosed T2DM. Thus, the prevalence of disease is likely underestimated (2, 3). Testing was performed at school between 0830 and 1000 h in early December and again in early April. Students and their parents were contacted the night before testing and reminded not to consume any foods or beverages except water on the morning of testing. Height, weight, and percent body fat by bioimpedance (Omron HBF-300; Omron Health Care, Inc., Vernon Hills, IL) were measured. A 21-gauge butterfly needle was inserted into an antecubital vein under local anesthesia with a 4% lidocaine cream (Elamax; Ferndale Laboratories Inc., Ferndale, MI). Blood was drawn for fasting concentrations of insulin, glucose, CRP, IL-6, TNF-α, ACRP30, cholesterol, triglycerides, and cholesterol subfractions; 0.5 mg/kg of glucose (50% dextrose, maximum 25 g) was then infused over 3 min via the indwelling butterfly needle and blood was drawn through the same indwelling line for measurement of serum insulin concentration at 3 and 5 min after glucose administration. After completion of testing, subjects were given breakfast and then escorted back to their usual classes. Insulin sensitivity and secretory capacity were assessed using, respectively, the quantitative insulin sensitivity check index (QUICKI) (11) and acute insulin response (AIR) (mean incremental rise in plasma insulin at 3 and 5 min after iv glucose) (11).

Intervention

The classroom intervention was integrated into the regular science program was taught by investigators (M.R., C.N., and R.W.). Classroom sessions were 45 min in duration and offered once per week. The first two classroom sessions were devoted to experimental design, diabetes epidemiology, and pathophysiology, and subject recruitment and occurred before initial testing. Sessions 3–8 (offered after initial testing) were devoted to nutrition education and diet modifications designed to lower dietary fat (especially saturated fat), sweetened sodas and juices, and "fast" or "supersized" food consumption, and encouragement to share this information with parents. Session 9 reviewed anonymous data from the initial study period with an emphasis on experimental design, ethics, responsibilities of scientists, and data analyses. Sessions 10–11 focused on the basic principles of thermodynamics and the importance of regular exercise. Sessions 12 and 13 reviewed the intervention material. Final data analyses and assistance in preparation of science projects were offered in session 14, after the study was completed.

The exercise program used in this study was specifically designed by investigators (M.R. and R.W.) and physical education teachers to be gender- and somatotype-neutral. All exercise sessions were supervised by an investigator (R.W.) and consisted of dance/noncontact kickboxing that was offered three times per weekly. Students had the option of attending the exercise intervention or attending regular gym classes. Attendance records were kept for all classrooms, all exercise, and all regular gym sessions.

Assays

Glucose was measured by the hexokinase method (Glucose/HK; Roche Molecular Biochemicals, Werk Penzberg, Federal Republic of Germany). Plasma insulin was measured by solid phase ^{125}I-RIA (Coat-a-count; DPC, Los Angeles, CA). Lipid profiles (cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein) were measured colorimetrically using an automated Hitachi 704 spectrometer. CRP, TNF-α, and total ACRP30 were determined by ELISA. IL-6 was assayed by RIA.

Statistics and calculations

Because insulin sensitivity and insulin release are significantly correlated (4), a glucose disposal index (GDI) was calculated as $\log_{10}$(AIR $\times$ fasting glucose concentration/fasting insulin concentration) to adjust AIR for insulin sensitivity as described previously (11). Between-groups comparisons were made by ANOVA. Within groups analyses were made by ANOVA with repeated measures. Initial comparisons (preintervention *vs.* postintervention and experimental *vs.* control groups) were made using the entire experimental group. Statistical significance was prospectively defined as $P_\alpha < 0.05$.

Results

Subject groups

Baseline data on 60 of 73 of the subjects have been included in a previously published data set (11). No significant differences were noted at baseline between control and experimental subjects (see Table 1). Fasting insulin, glucose, and inflammatory and lipid profiles were obtained from all subjects, but full rapid iv glucose tolerance testing was completed at both testing sessions in 55 of 73 subjects. Incomplete data sets occurred because at one or both testing sessions there was poor venous access (n = 7), requests by students to stop the test because they felt nauseated (n = 3), or requests by students to measure only fasting bloods (n = 8).

Intervention

After the intervention, percentage body fat, BMI, and circulating concentrations of CRP were significantly lower, and QUICKI was significantly higher in experimental compared with control subjects and in experimental subjects compared with themselves before the intervention (see Table 1 and Fig. 1). Neither gender nor initial somatotype was significant covariates of these effects. Gym or exercise intervention attendance was generally very good (60 of 73 students attended and participated in physical education classes on the average of at least twice per week) in both control and experimental groups.

Whereas participation in the classroom portion of the intervention was mandatory, students voluntarily elected whether to participate in the exercise portion of the study. Lack of participation in the exercise program was defined as electing to take regular gym rather than the intervention and taking the intervention exercise class for less than one of the three sessions offered each week. Using this definition, the instruction-only group consisted of 29 students, and the instruction and exercise group consisted of 20 students. No significant between group differences were noted in gender distribution, frequency of relatives with T2DM, lipid profiles, inflammatory marker profiles, or GDI, nor in the frequency of classroom of gym attendance. BMI and percent body fat were significantly higher in the group of students who participated in both classroom and exercise instruction (BMI = 23.0 $\pm$ 1.0 kg/m^2 and % body fat = 23.6 $\pm$ 1.6% in classroom only group *vs.* 25.8 $\pm$ 1.7 kg/m^2 and 25.5 $\pm$ 0.16% in the classroom and exercise group, both $P < 0.05$). As expected from the observation that the classroom and exercise participation group was significantly fatter, AIR was significantly higher and QUICKI was significantly lower in the students in classroom and exercise group (QUICKI = 0.34 $\pm$ 0.01 and AIR = 640 $\pm$ 90 mU/ml in classroom only group *vs.* 0.33 $\pm$ 0.01 and 1190 $\pm$ 157 mU/ml in the classroom and exercise group, both $P < 0.05$). Group differences in these

TABLE 1. Anthropometric and laboratory data

	Control (n = 24)		Experimental (n = 49)	
	Test 1	Test 2	Test 1	Test 2
Male/female	14/10		28/21	
Age (yr)	13.6 ± 0.2		13.7 (0.1)	
FH T2DM	53%		53%	
Weight (kg)	64.6 ± 5.6	65.9 ± 5.7	66.7 ± 3.2	66.6 ± 3.1
BMI (kg/m^2)	24.3 ± 1.8	24.8 ± 1.9	24.7 ± 1.4	24.0 ± 1.5[a]
% Body fat	25.8 ± 3.7	27.4 ± 3.1	24.4 ± 1.4	23.1 ± 1.4[a]
Cholesterol (mg/dl)	137 ± 5	141 ± 6	155 ± 5	157 ± 5
(mmol/liter)	(3.55 ± 0.13)	(3.66 ± 0.16)	(4.01 ± 0.12)	(4.06 ± 0.14)
Triglyceride (mg/dl)	86 ± 5	82 ± 7	91 ± 9	87 ± 8
(mmol/liter)	(0.97 ± 0.06)	(0.93 ± 0.08)	(1.03 ± 0.10)	(0.98 ± 0.06)
HDL (mg/dl)	57 ± 5	58 ± 7	48 ± 2	47 ± 2
(mmol/liter)	(1.48 ± 0.13)	(1.50 ± 0.18)	(1.24 ± 0.07)	(1.22 ± 0.09)
LDL (mg/dl)	85 ± 3	82 ± 6	89 ± 4	93 ± 3
(mmol/liter)	(2.20 ± 0.08)	(2.12 ± 0.16)	(2.31 ± 0.11)	(2.41 ± 0.08)
Glucose (mg/dl)	84 ± 1	84 ± 1	85 ± 1	84 ± 1
(mmol/liter)	(4.67 ± 0.06)	(4.67 ± 0.06)	(4.68 ± 0.06)	(4.67 ± 0.06)
Insulin (mU/ml)	15 ± 3	14 ± 3	16 ± 3	15 ± 3
(pmol/liter)	(104 ± 21)	(97 ± 21)	(111 ± 23)	(104 ± 22)
QUICKI	0.33 ± 0.01	0.33 ± 0.01	0.33 ± 0.01	0.35 ± 0.01[a]
AIR (mU/ml)	961 ± 104 (n = 16)	937 ± 129 (n = 16)	866 ± 140 (n = 39)	924 ± 159 (n = 39)
(pmol/liter)	6659 ± 720	6493 ± 894	6001 ± 970	6556 ± 1101
GDI	3.5 ± 0.1 (n = 16)	3.6 ± 0.1 (n = 16)	3.6 ± 0.1 (n = 39)	3.6 ± 0.1 (n = 39)
CRP (pg/ml)	3.03 ± 1.15	3.02 ± 1.25	2.72 ± 0.81	1.60 ± 0.98[a,b]
TNF-α (pg/ml)	1.21 ± 0.15	1.24 ± 0.18	1.54 ± 0.14	1.55 ± 0.13
IL-6 (pg/ml)	0.96 ± 0.19	0.91 ± 0.17	1.16 ± 0.15	0.86 ± 0.15[a]
ACRP30 (μg/ml)	9.98 ± 1.71	9.65 ± 1.70	9.54 ± 1.07	9.93 ± 1.12

There were no significant differences between groups at enrollment. Participation in the intervention was associated with a significant increase in QUICKI and a significant decrease in BMI and % body fat, as well as circulating concentrations of CRP and IL-6. FH, Family history.

[a] $P < 0.05$ compared with initial testing.

[b] $P < 0.05$ compared with control group.

values were no longer significantly different when corrected by ANCOVA for body fatness.

No statistically significant differences between groups were noted in the effects of the intervention of T2DM risk factors and attendance was not a significant covariate of the overall effect of participation in the intervention (see Fig. 1). Examination of intervention effects on circulating concentrations of IL-6 and CRP found that whereas circulating concentrations of these inflammatory markers were lower in all experimental subsets compared with controls, statistical significance was achieved only in the group participating in both the classroom and exercise interventions.

Discussion

Our major finding is that body fatness, insulin resistance, and circulating concentrations of IL-6 and CRP can be significantly reduced in adolescents through a school-based intervention, regardless of initial gender or somatotype. Other studies of school-based interventions using only body fatness as the major outcome variable, without significant out of school activities such as personal or family counseling or repeated clinic visits have reported little or no effect on BMI (12, 13) even though health knowledge (14) and, in some studies, insulin sensitivity (15) increase. Prospective studies of lifestyle intervention on diabetes risk have suggested that that classroom health education improves food choices, body fatness, and insulin resistance but have targeted specific populations of individuals already known to be "at risk" for T2DM by virtue of being overweight or having impaired glucose tolerance or gestational DM (16). In this study, risk factors for T2DM included an array of biochemical and clinical factors and the intervention was not limited to any specific "at-risk" group. The inclusion of these biochemical markers of health and diabetes risk increases the sensitivity of this study, and demonstrates that a school-based intervention can improve student health at multiple levels. The inclusion of children outside of those "at risk" by virtue of being overweight or already demonstrating abnormal glucose homeostasis, avoids any stigmatization of overweight children and demonstrates that this type of intervention is beneficial to all students.

These data suggest beneficial and additive effects of lifestyle and exercise interventions on diabetes risk. The association of weight reduction with improved insulin sensitivity in overweight children (15) and the independent additive beneficial effects of weight loss and exercise on insulin sensitivity in adults (17) have been reported previously. Lifestyle only interventions significantly decrease circulating concentrations of CRP and IL-6 in adolescents (18), whereas increased physical activity is associated with higher insulin sensitivity (19). The lack of significant differences in intervention benefits between subjects participating only in the classroom intervention *vs.* both the classroom and exercise intervention must be interpreted cautiously. Students participating in the classroom only and classroom and exercise groups were self-selected and were in the same classes, raising the possibility that the improvement in these variables in the classroom only group was a reflection of increases in

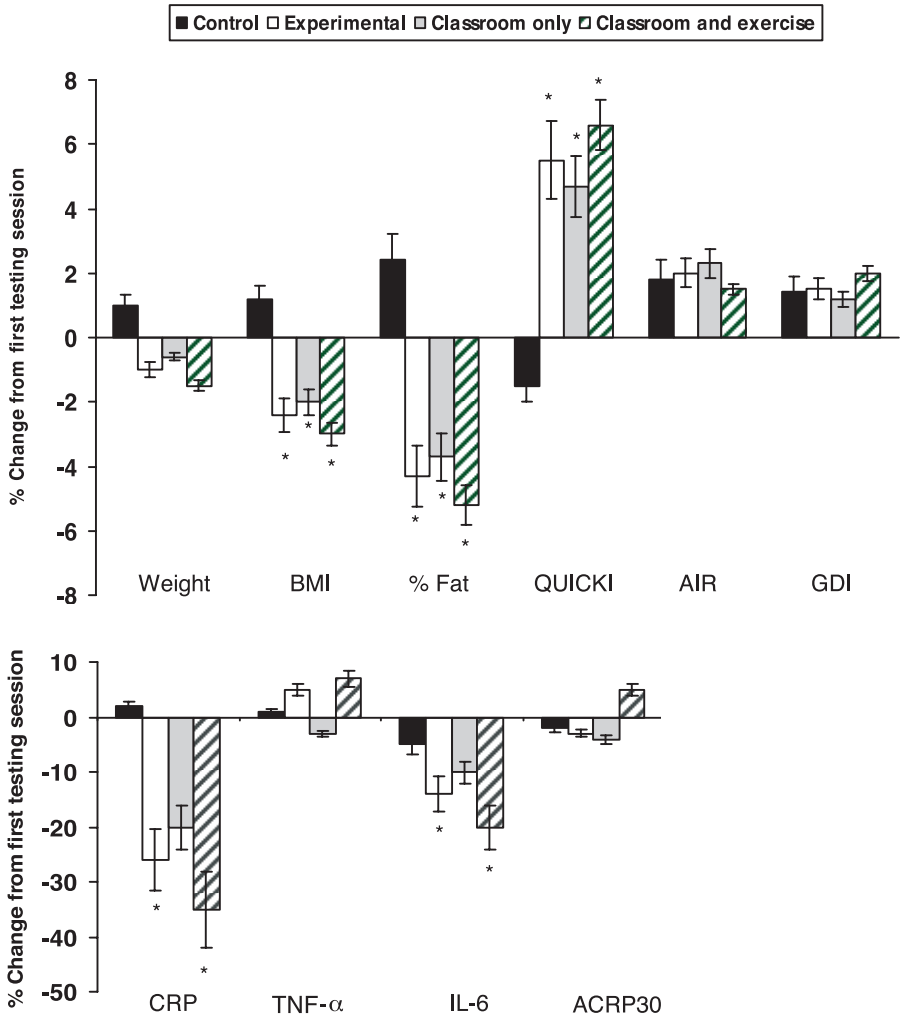

FIG. 1. Mean (SEM) percent change in body composition, glucose homeostasis, and inflammatory markers between testing sessions in control subjects (*black bars*), all experimental subjects (*open bars*), and subsets of experimental subjects who participated only in the classroom portion of the intervention (*gray bars*) or both the classroom and exercise portions of the interventions (*striped bars*). *, $P < 0.05$ compared with control.

physical activity that were initiated by association with other students. No accurate before/after quantification of time spent in physical activity, the level of physical activity performed, or diet composition changes as a result of the intervention were made to further examine this issue. Furthermore, the size of the physical education classes for the students in the classroom only group was significantly reduced simply by virtue of the fact that some of their classmates were participating in the aerobic exercise program. The smaller gym class may also have resulted in increased physical activity for all participants.

This type of productive collaboration between health professionals, teachers, school administrators, and students demonstrates the specific biochemical and clinical benefits of a school-based intervention intended to reduce body fatness and T2DM risk factors. Without reinforcement, it is unlikely that these benefits would persist over time. The potential benefits of early intervention and need for a sustained program are illustrated by the Kahnawake Schools Diabetes Prevention Project (20), in which 6- to 11-yr-old children received a health-oriented curriculum plus community intervention resulting in significant improvement in diabetes risk (BMI, diet, sedentary activity, and skinfold thicknesses) while the program was operant. However, these benefits were not sustained 2 yr after the intervention stopped. Longer-term studies of similar interventions should evaluate the most effective and easily implemented lifestyle modifications to produce and maintain the effects seen in our study. It is a reasonable inference that this type of instruction, given as part of the regular school curriculum, would reduce diabetes risk throughout school and perhaps beyond.

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