# Weight, Adiposity, and Physical Activity as Determinants of an Insulin Sensitivity Index in Pima Indian Children

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**OBJECTIVE** — To determine whether measures of physical activity are related to an insulin sensitivity index ([ISI] $10^4$/fasting insulin × glucose) independent of weight or adiposity in children.

**RESEARCH DESIGN AND METHODS** — We conducted a longitudinal study of 90 Pima Indian children (39 boys and 51 girls) at 5 and 10 years of age measuring adiposity (dual-energy X-ray absorptiometry), physical activity behavior (questionnaire: number of activities per week [ACT], average hours per week [TIME]), and energy expenditure (doubly labeled water: physical activity level [PAL]).

**RESULTS** — In cross-sectional analyses, ACT was correlated with ISI at 5 years of age ($r = 0.24$, $P = 0.02$) and at 10 years of age ($r = 0.21$, $P = 0.05$), but these relationships were not independent of weight or adiposity. PAL was correlated with ISI at 10 years of age ($r = 0.39$, $P = 0.03$) but was not independent of weight or adiposity. Longitudinally, ISI decreased from 5 to 10 years of age, and increases in weight and adiposity were associated with decreases in ISI ($r = -0.51$ and $-0.41$, respectively; both $P < 0.0001$). ACT decreased from 5 to 10 years of age, but children who had smaller decreases in ACT had smaller decreases in ISI, independent of increases in weight or adiposity (partial $r = 0.22$, $P = 0.04$ adjusted for either weight or adiposity).

**CONCLUSIONS** — These data suggest that early establishment and maintenance of an active lifestyle can have a beneficial effect on ISI that is partially independent of changes in weight or adiposity. This is particularly relevant considering the current epidemics of both obesity and type 2 diabetes in children.

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Obesity is a well-documented risk factor for insulin resistance and type 2 diabetes in adults (1) and has also been associated with insulin resistance and the development of impaired glucose tolerance in children and adolescents (2). Among the Pima Indians, a population with the highest reported prevalence of type 2 diabetes in the world (3), many children are markedly overweight at both 5 and 10 years of age (4).

Chronically low levels of physical activity are believed to contribute to the increasing prevalence of obesity in children (5). A recent report on Pima Indian children from our laboratory suggests that children who do not increase their physical activity energy expenditure (AEE) in proportion to weight gain during growth are at greater risk for obesity (6).

Acute exercise is known to transiently improve insulin sensitivity (7), and exercise training studies have reported increases in insulin sensitivity along with decreases in body fat both in adults (8) and in children (9). Whether habitual levels of physical activity are associated with insulin sensitivity independent of adiposity is less clear, but physical activity has been proposed as a modifiable risk factor for development of type 2 diabetes (10). Dengel et al. (11) reported that 10 months of aerobic training and weight loss had additive effects on improving glucose homeostasis in obese sedentary men, suggesting that physical activity and adiposity have independent mechanisms for altering insulin sensitivity. Cross-sectional associations between insulin sensitivity and physical activity levels independent of adiposity have been reported in children and adolescents (12,13), and an association of physical activity with insulin levels independent of BMI was recently reported in Pima Indian adults (14). Considering the difficulty of treating childhood obesity, as well as the increase in adiposity that was observed in Pima Indian children between 5 and 10 years of age (6), it is important to determine whether changes in physical activity during this time had an independent impact on changes in insulin sensitivity.

The aims of this study were to evaluate the cross-sectional and longitudinal relationships of an insulin sensitivity index (ISI) with body weight, adiposity, and measures of physical activity at 5 and 10 years of age as well as the extent to which the relationship between physical activity and ISI is independent of body weight and/or adiposity. Whereas fasting plasma insulin concentrations increase through childhood to support growth, evaluating the relative changes in the fasting plasma concentrations of insulin and glucose with an ISI equation gives an indication of changes in insulin sensitivity. We hypothesized that children with higher levels of physical activity would have a higher ISI

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**Abbreviations:** ACT, activities per week; AEE, activity energy expenditure; DLW, doubly labeled water; GLM, general linear model; ISI, insulin sensitivity index; PAL, physical activity level; RMR, resting metabolic rate; TEE, total energy expenditure; TIME, average hours per week.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

than less active children and that this association is partly independent of weight or adiposity. We further hypothesized that although a decrease in ISI is associated with an increase in weight or adiposity from 5 to 10 years of age, there is less of a decrease in those children who remain relatively more active.

## RESEARCH DESIGN AND METHODS

### Subjects

Children were participants in a longitudinal study of the pathophysiology of obesity and type 2 diabetes in the Pima Indian population (4). Data reported here ($n = 90$; 39 boys and 51 girls) were collected during the summer months when subjects were 5 and 10 years of age. Briefly, children were studied at the National Institutes of Health field clinic located in the Gila River Indian Community in Sacaton, Arizona, ~40 miles southeast of Phoenix. Subjects were of full Indian and at least 75% Pima-Tohono-O'Odham heritage. Children arrived at the clinic at 0800 in a fasted state, accompanied by one of their parents, and their health status was determined by medical history and physical examination. Before participation, volunteers and their parents were fully informed of the nature and purpose of the study, and written informed consent/assent was obtained. The experimental protocol was approved by the Institutional Review Board of the National Institute of Diabetes and Digestive and Kidney Diseases and the Tribal Council of the Gila River Indian Community.

### Anthropometry and body composition measurements

Anthropometric measurements were recorded in all children at 5 and 10 years of age. Height and weight were measured without shoes while the children were wearing light summer clothing. BMI was calculated as the ratio of body weight and squared height. Body composition was determined using dual-energy X-ray absorptiometry as described previously (15).

### Measurement of physical activity

Two methods of measuring physical activity were used in this study.

***1*) Measurement of energy expenditure.** Total energy expenditure (TEE) was determined using doubly labeled water (DLW) combined with measurement of resting metabolic rate (RMR) by indirect calorimetry. These variables were then used to calculate: *1*) AEE = TEE − (RMR + 0.1 × TEE), where 0.1 × TEE represents an estimate of the thermic effect of food (16); and *2*) physical activity level (PAL) = TEE/RMR. The DLW method required having the subjects provide one baseline urine sample that had been collected at home the evening before the test. Upon arrival at the clinic on the first study day, a second baseline urine sample was collected before children were dosed with DLW as previously described (17). Complete urine collections were made at ~1.5, 2.5, 3.5, and 4.5 h after dosing on day 1 and twice during a 3-h period 7 days later. This assessment was made in all 5-year-old children but could only be measured in 33 of the 90 children at 10 years of age (follow-up) due to a worldwide shortage of DLW (18). After ingesting the DLW, children rested comfortably on a bed for 10 min, after which the RMR was measured for 20 min using a DeltaTrac Metabolic Monitor (SensorMedics, Yorba Linda, CA) as previously described (19). The RMR measurement was repeated at the return visit 1 week later, and the results of the two measurements were averaged to obtain the mean of the two values for all 5-year-old children and 33 children at follow-up. In the remaining 57 children at follow-up (10 years old), the RMR measurement was made only once but was conducted for a 25-min period.

**2) Measurement of physical activity behavior.** A physical activity questionnaire, completed by the parent, was used to assess average hours per week (TIME) and number of activities per week (ACT) during the previous year in which the child was typically engaged in sports and recreational activities that required a greater expenditure of energy than that normally needed for daily grooming, bathing, and eating (20).

### Analytical procedures

Morning blood samples were collected after a 10-h overnight fast for the determination of plasma glucose and insulin concentrations. Plasma glucose concentrations were measured using the glucose oxidase method (Beckman Instruments, Fullerton, CA); the intra- and interassay coefficients of variation (CVs) were 1.6 and 2.9%, respectively. Plasma insulin concentrations were determined by automated immunoassay (Access; Beckman Instruments); intra- and interassay CVs were 2.6 and 4%, respectively.

### Calculated ISI

Fasting plasma glucose and insulin concentrations were used in the following equation for calculating an ISI: $10^4$/[insulin (μU/ml) × glucose (mg%)] (21).

### Statistical methods

All statistical analyses were performed using SAS software (SAS Institute, Cary, NC). Data are expressed as means ± SD. Fasting insulin concentrations and the ISI were log-transformed ($\log_{10}$) to approximate a normal distribution.

### Cross-sectional analyses

Sex differences in anthropometric, metabolic, and physical activity variables at 5 and 10 years of age were evaluated using Student's *t* tests. Pearson correlation coefficients were used to quantify the relationship of the physical activity variables with each other as well as with ISI at 5 and 10 years of age. A general linear model (GLM) was separately applied to evaluate each of the anthropometric variables (body weight or percent body fat) with each of the physical activity variables (ACT or TIME or AEE or PAL) as determinants of insulin sensitivity at 5 and 10 years of age after adjusting for sex.

### Longitudinal analyses

Unadjusted relationships between changes in ISI with changes in physical activity or changes in weight or adiposity were evaluated by Pearson correlation coefficients. GLM equations were used to determine the relationship of changes in insulin sensitivity with changes in each physical activity variable after adjusting for sex and changes in weight or percent body fat.

## RESULTS

### Subject characteristics

From 5 to 10 years of age, there was an overall increase in fasting plasma insulin concentrations, percent body fat, and unadjusted measures of energy expenditure (AEE and PAL) and decreases in ISI and physical activity behavior (TIME and ACT; $P < 0.01$ for ACT and $P < 0.0001$ for age-related changes in all other variables) (Table 1). When compared by sex, boys were taller ($P < 0.05$) and had

**Table 1—*Subject characteristics at 5 and 10 years of age***

| Variable | Total ($N$ = 90) 5 years | Total ($N$ = 90) 10 years | Boys ($n$ = 39) 5 years | Boys ($n$ = 39) 10 years | Girls ($n$ = 51) 5 years | Girls ($n$ = 51) 10 years |
|---|---|---|---|---|---|---|
| Age (years) | 5.5 ± 0.3 | 10.5 ± 0.3 | 5.6 ± 0.3 | 10.5 ± 0.3 | 5.5 ± 0.3 | 10.5 ± 0.3 |
| Weight (kg) | 23.5 ± 5.1 | 54.5 ± 13.9 | 24.0 ± 4.7 | 53.4 ± 13.6 | 23.0 ± 5.4 | 55.0 ± 14.5 |
| Height (cm) | 115 ± 4 | 147 ± 6 | 116 ± 4† | 147 ± 6 | 114 ± 4† | 148 ± 6 |
| BMI (kg/m$^2$) | 17.6 ± 3.0 | 24.9 ± 5.4 | 17.8 ± 2.9 | 24.7 ± 5.3 | 17.5 ± 3.1 | 25.0 ± 5.6 |
| Body fat (%) | 30.4 ± 7.3 | 40.6 ± 8.3 | 29.0 ± 7.3 | 38.7 ± 8.1 | 31.5 ± 7.2 | 42.0 ± 8.3 |
| Glucose (mg%) | 80 ± 7 | 93 ± 8 | 81 ± 6 | 80 ± 7 | 93 ± 8 | 92 ± 7 |
| Insulin ($\mu$U/ml) | 21 ± 10 | 55 ± 34 | 23 ± 9 | 44 ± 21* | 20 ± 11 | 62 ± 39* |
| ISI ($10^{+}$/glu × ins) | 81 ± 20 | 36 ± 23 | 96 ± 17 | 70 ± 12† | 103 ± 20 | 64 ± 11† |
| ACT (number per week) | 5.8 ± 2.6 | 4.0 ± 2.1 | 5.3 ± 2.7 | 4.2 ± 2.2 | 6.0 ± 2.6 | 3.9 ± 2.0 |
| TIME (hours per week) | 14.6 ± 12 | 11.0 ± 10.1 | 14.6 ± 12.3 | 11.7 ± 10.1 | 14.1 ± 11.7 | 9.4 ± 9.1 |
| | | | $n$ = 16 | | $n$ = 17 | |
| AEE (kJ/d) | 1,038 ± 549 | 2,790 ± 741 | 1,208 ± 511* | 2,841 ± 610 | 896 ± 543* | 2,602 ± 655 |
| PAL (TEE:RMR) | 1.37 ± 0.13 | 1.59 ± 0.13 | 1.40 ± 0.12† | 1.58 ± 0.11 | 1.35 ± 0.14† | 1.58 ± 0.14 |

Data are means ± SD. *$P < 0.01$; †$P < 0.05$ for sex differences.

higher levels of energy expenditure (AEE, $P < 0.01$; PAL, $P < 0.05$) at 5 years of age than girls. At 10 years of age, girls had higher fasting plasma insulin concentrations ($P < 0.01$) and lower ISI ($P < 0.05$).

### Relationships between physical activity variables

The physical activity behavior variables (ACT and TIME) were correlated ($P < 0.05$) with each other at 5 years ($r = 0.23$) and at 10 years ($r = 0.21$). The energy expenditure variables (AEE and PAL) were also correlated ($P < 0.0001$) with each other at 5 years ($r = 0.97$) and at 10 years ($r = 0.88$). Correlations for each physical activity variable with itself at 5 vs. 10 years of age were significant for ACT ($r = 0.28$, $P < 0.01$), TIME ($r = 0.35$, $P < 0.001$), and AEE ($r = 0.44$, $P < 0.01$). The relationship between TIME and PAL at 10 years of age was the only significant correlation between a behavioral and energy expenditure variable ($r = 0.36$, $P < 0.05$).

### Physical activity and ISI

**Cross-sectional analyses.** Because the statistical relationships of ISI with both ACT and TIME as well as with both AEE and PAL were similar, results for the associations between physical activity levels and ISI are presented only for the physical activity behavior variable ACT (number per week) and the energy expenditure variable PAL (TEE:RMR). ACT was positively related to ISI (adjusted for sex) at both 5 years of age ($r = 0.24$, 95% CI 0.03–0.43; $P = 0.02$) and at 10 years of age (0.21, 0.003–0.40; $P = 0.05$), whereas the relationship between PAL and ISI was significant (0.39, 0.05–0.65; $P = 0.03$, $n = 33$) only at 10 years of age. There was no relationship between PAL and ISI at 5 years of age (−0.06, −0.24 to 0.15; $P = 0.61$, $n = 90$). Weight and percent body fat were each strong negative determinants of ISI at both 5 and 10 years of age. Once adjusted for either of these anthropometric variables and sex, the physical activity variables were not independent determinants of ISI (Table 2).

**Longitudinal analyses.** Increases in either weight or percent body fat were associated with the decreases in ISI that were observed in these children from 5 to 10 years of age (Fig. 1*A* and *B*). When changes in ISI were adjusted for sex and increases in weight or adiposity (Table 3, Fig. 1*C*), children with greater decreases in ACT from 5 to 10 years of age also had greater decreases in ISI, independent of weight or adiposity changes (partial $r = 0.22$, 0.01–0.41; $P = 0.04$, $n = 90$). There were no significant associations between changes in PAL and changes in ISI, either unadjusted or adjusted for changes in weight (partial $r = 0.11$, −0.24 to 0.44; $P = 0.55$, $n = 33$) or adiposity (Table 3, Fig. 1*D*).

**CONCLUSIONS** — ISI decreased during childhood in Pima Indians and levels and changes in weight or adiposity were strong negative determinants of levels and changes in ISI, respectively. Although physical activity behavior was positively associated with ISI at 5 years of age and both physical activity behavior and energy expenditure were associated with ISI at 10 years of age, cross-sectional relationships were dependent on weight or adiposity. Although physical activity behavior decreased from 5 to 10 years of age, children who remained relatively more active had smaller decreases in ISI, which was partly independent of increases in weight or adiposity.

### Changes in insulin sensitivity during childhood in Pima Indians

There was a decrease in ISI from 5 to 10 years of age, and levels were lower in girls than boys at 10 but not at 5 years of age. This is in agreement with cross-sectional (22,23) and longitudinal (24) studies in other groups of children. The reason for the sex difference in this group could be due to maturational differences and the well-documented increase in insulin resistance with puberty (25,26). Guzzaloni et al. (23) reported that insulin sensitivity decreased in both sexes during puberty but that decreases occurred earlier in girls than boys. Although we did not measure Tanner stages in this group, it is reasonable to assume that the girls in this study were more mature at 10 years of age than the boys (27).

### Insulin sensitivity and physical activity

Physical activity was weakly associated with ISI in cross-sectional analyses. The unadjusted association of the behavioral variable ACT with ISI was significant at both 5 and 10 years of age, but for the

**Table 2**—*Determinants of ISI at 5 and 10 years of age*

| | 5 years | | | 10 years | | |
|---|---|---|---|---|---|---|
| Dependent variable = ISI | Estimate (β) | SE | *P* value | Estimate (β) | SE | *P* value |
| | | *n* = 90 | | | *n* = 90 | |
| *Model 1* | | | | | | |
| Weight (kg) | −0.016 | 0.004 | <0.0001 | −0.011 | 0.001 | <0.0001 |
| Sex (male versus female) | 0.040 | 0.038 | 0.27 | −0.106 | 0.035 | 0.004 |
| ACT (number per week) | 0.010 | 0.007 | 0.16 | 0.006 | 0.009 | 0.46 |
| *Model 2* | | | | | | |
| Percentage body fat | −0.011 | 0.003 | <0.0001 | −0.015 | 0.002 | <0.0001 |
| Sex | 0.085 | 0.038 | 0.03 | −0.067 | 0.040 | 0.10 |
| ACT | 0.014 | 0.007 | 0.06 | 0.013 | 0.010 | 0.20 |
| | | *n* = 90 | | | *n* = 33 | |
| *Model 3* | | | | | | |
| Weight | −0.018 | 0.004 | <0.0001 | −0.010 | 0.003 | 0.001 |
| Sex | 0.052 | 0.039 | 0.18 | −0.105 | 0.066 | 0.12 |
| PAL (TEE:RMR) | 0.125 | 0.150 | 0.41 | 0.392 | 0.256 | 0.14 |
| *Model 4* | | | | | | |
| Percentage body fat | −0.011 | 0.003 | <0.0001 | −0.012 | 0.004 | 0.01 |
| Sex | 0.096 | 0.040 | 0.02 | −0.063 | 0.070 | 0.38 |
| PAL | 0.059 | 0.150 | 0.69 | 0.493 | 0.270 | 0.07 |

energy expenditure variable (PAL), the relationship was significant only at 10 years of age. Other studies have demonstrated an association between either physical activity or fitness level with insulin sensitivity (8–11,28). However, in children, it is not certain whether physical activity has an independent impact on insulin physiology or whether it works solely through changes in levels of adiposity. In our study, physical activity was a significant determinant of the ISI only when not adjusted for either weight or percent body fat. This is in contrast to other studies that have reported associations between physical activity or fitness levels and measures of insulin sensitivity independent of various measures of body mass or body composition in adults (11,14,29) and children (12,13,28). None of the studies in children, however, used DLW to measure physical activity level but instead used $V\text{O}_{2\text{max}}$ (12,28) and/or questionnaire variables (12,13). Although we did not find an independent cross-sectional association between physical activity and ISI, it is possible that the range of physical activity levels was too limited to be statistically significant in our cohort.

In longitudinal analyses, we observed an association between changes in physical activity behavior (ACT) during childhood and changes in ISI independent of sex and changes in weight or adiposity. This finding is consistent with what is known about the chronic effects of exercise on insulin sensitivity. Whereas acute exercise increases skeletal muscle glucose uptake through both insulin-dependent and -independent mechanisms, the effects only last up to ~24 h (7). Chronic or habitual exercise (training) improves whole-body insulin sensitivity not only through increases in absolute or relative fat-free mass but also through increased capillary density for improved glucose delivery and increased synthesis of GLUT4 transporter proteins and other components of the insulin signaling system (7).

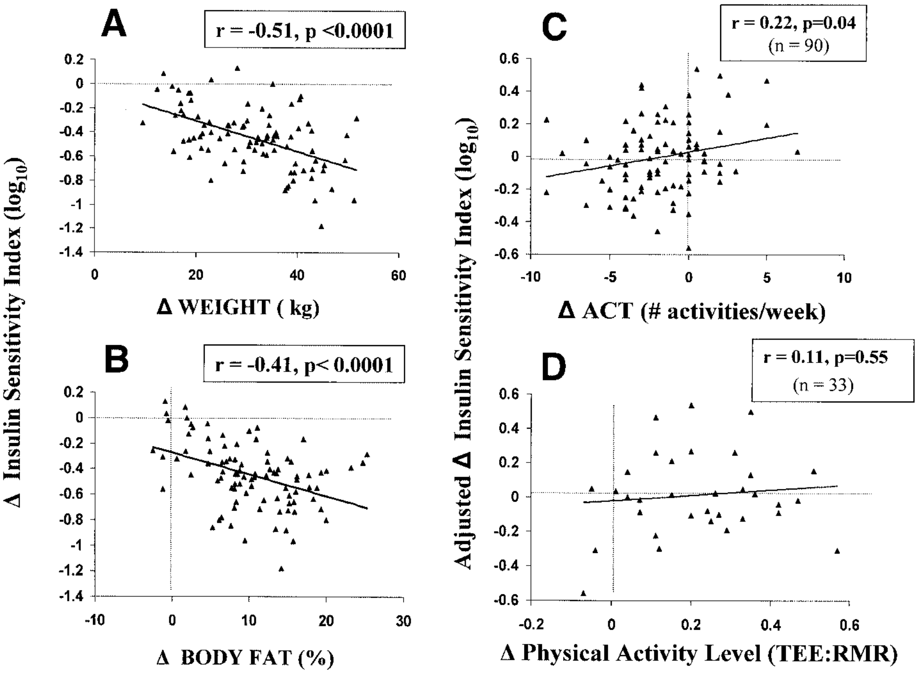

**Figure 1**—*Relationships between the change (from 5 to 10 years of age) in the ISI and changes in weight* (A) *and percent body fat* (B), *as well as change in the ISI (adjusted for sex and change in weight) and changes in number of ACT* (C) *and PAL* (D).

**Table 3**—***Determinants of longitudinal changes in ISI (ΔISI) from 5 to 10 years of age***

| Dependent variable = ΔISI | Estimate (β) | SE | *P* value |
|---|---|---|---|
| | | *n* = 90 | |
| *Model 1* | | | |
| ΔWeight (kg) | −0.012 | 0.002 | <0.0001 |
| Sex (male versus female) | −0.146 | 0.044 | 0.001 |
| ΔACT (number per week) | 0.015 | 0.007 | 0.04 |
| *Model 2* | | | |
| ΔPercentage body fat | −0.016 | 0.004 | <0.0001 |
| Sex | −0.166 | 0.047 | 0.001 |
| ΔACT | 0.016 | 0.008 | 0.04 |
| | | *n* = 33 | |
| *Model 3* | | | |
| ΔWeight | −0.010 | 0.005 | 0.06 |
| Sex | −0.191 | 0.080 | 0.02 |
| ΔPAL (TEE:RMR) | 0.248 | 0.282 | 0.32 |
| *Model 4* | | | |
| ΔPercentage body fat | −0.023 | 0.007 | 0.004 |
| Sex | −0.186 | 0.074 | 0.02 |
| ΔPAL (TEE:RMR) | 0.242 | 0.246 | 0.33 |

These training adaptations, however, are only maintained as long as exercise is performed on a regular basis (30). Therefore, any longitudinal benefits that exercise might have on improving insulin sensitivity require maintenance of some level of physical activity.

In the current study, physical activity behavior decreased from 5 to 10 years of age, whereas measures of energy expenditure increased. The unadjusted increases in AEE and PAL reflect an increase in weight and adiposity. Both physical activity behavior variables (ACT and TIME) and the energy expenditure variable (AEE) were significantly correlated between 5 and 10 years of age, suggesting that physical activity patterns begin to track as early as 5 years of age. Children who had greater longitudinal decreases in ACT (number per week) from 5 to 10 years of age had greater decreases in ISI, even after adjusting for increases in weight or adiposity, a finding that illustrates the importance of maintaining or increasing levels of habitual physical activity.

## Limitations

There are limitations in the methodologies used in these children to assess insulin sensitivity and PALs. Although the hyperinsulinemic-euglycemic clamp is the "gold standard" for measuring whole-body insulin sensitivity, this is an expensive, invasive, and cumbersome technique, especially in children. In this study, insulin sensitivity was calculated from fasting plasma insulin and glucose concentrations in an equation previously correlated with clamp data in Pima Indian adults ($r = 0.60$, $P < 0.0001$) (21). Because we do not perform clamp studies in Pima Indian children, we were unable to validate the equation specifically for children as it was done in adults. However, in many other studies, fasting plasma insulin and glucose concentrations have been used to calculate insulin resistance (31,32) or insulin sensitivity (33,34), and these measures have shown good agreement with clamp, intravenous glucose tolerance test, or oral glucose tolerance test measurements in children (22,23,24). The strong correlation between various measures of assessing insulin sensitivity is likely to reflect the fact that they apply similar models to the relationship of insulin to glucose under fasting conditions (35), but measures based solely on fasting insulin and glucose levels require stronger assumptions and are potentially influenced by additional determinants of insulin sensitivity.

There has been much discussion in the literature regarding the most relevant method of assessing physical activity in children when trying to evaluate its impact on variables such as adiposity or insulin sensitivity (36). The measurement of TEE by the DLW method is the gold standard, and when combined with measures of the resting metabolic rate, AEE and PAL can be calculated. Although the DLW method may be useful for assessing cross-sectional relationships between energy expenditure and weight or adiposity, whether this measurement is useful in prospective or longitudinal studies is not certain. Indeed, a prospective study in children reported that the fitness measurement $V\text{O}_{2\text{max}}$ predicted future adiposity, but measures of energy expenditure from the DLW method did not (37). Furthermore, measurement of energy expenditure may not capture aspects of activity such as mode or intensity, which may be more important for stimulating the physiological training adaptations that lead to improved insulin sensitivity (38,39). For example, the DLW method does not distinguish between weight-bearing and non–weight-bearing activity or between exercise and nonexercise activity, such as fidgeting (40).

Although questionnaires are highly subjective and depend on accurate recall or judgement, studies comparing measures of activity from questionnaires versus DLW in adults (41) and children (42) have concluded that questionnaires are adequate for population or group results but not for individuals. In the present study, none of the questionnaire variables were correlated with DLW variables at 5 years of age, whereas at 10 years of age there was only agreement between PAL and TIME. This suggests that the DLW and activity questionnaire methods may indeed measure different components of physical activity (i.e., a measure of energy expenditure versus patterns of physical activity behavior, respectively).

To our knowledge, this is the first longitudinal study in children to directly compare the DLW method with an activity questionnaire method for assessing relationships between changes in physical activity and changes in an ISI. Based on the present data, it seems that questionnaire variables, which measure activity behaviors, may be better than DLW at capturing the habitual or qualitative aspects of physical activity that have a long-term impact on ISI. It is also possible that the DLW measurement of energy expenditure over 1 week may not reflect levels of habitual physical activity throughout the year. However, the lack of a significant longitudinal relationship between PAL and ISI may be due to difference in sample size because it was not possible to measure PAL in all our subjects at 10 years of age due to a worldwide shortage of DLW (18). In fact, the 95% CI for the correlation coefficient between changes in PAL and changes in ISI are consistent with an effect as strong as that observed with changes in behavioral activity (ACT).

Despite these limitations, what we can conclude is that ISI decreases in Pima Indian children from 5 to 10 years of age and these levels and decreases are most strongly related to gains in weight and adiposity. Although physical activity behavior decreased from 5 to 10 years of age, children who were more active at 5 years of age tended to be relatively more active at 10 years of age, suggesting that patterns of habitual activity were already established in this group as early as 5 years of age. Most importantly, children who remained relatively more active during childhood had smaller decreases in the ISI, which were partly independent of changes in weight or adiposity. Whereas prevention and treatment of obesity is still of paramount importance for these children, the early establishment and maintenance of an active lifestyle can have some beneficial effect on ISI, regardless of degree of adiposity. This is particularly important not only for these obese children but for all children, considering the current epidemics of both childhood obesity and type 2 diabetes.

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