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PEDIATRIC BRIEF COMMUNICATION

Cardiovascular fitness and physical activity in children with and without impaired glucose tolerance

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Objective: To examine differences in cardiovascular fitness (VO_{2max}) and physical activity levels in overweight Hispanic children with normal glucose tolerance (NGT) vs impaired glucose tolerance (IGT).
Participants: A total of 173 overweight (BMI percentile 97.0 ± 3.1) Hispanic children ages 8–13 years with a family history of type 2 diabetes.
Methods: VO_{2max} was measured via a maximal effort treadmill test and open circuit spirometry. Physical activity was determined by questionnaire. Glucose tolerance was established by a 2-h oral glucose challenge (1.75 g of glucose/kg body weight). IGT was defined from an oral glucose tolerance test as a 2-h plasma glucose level $\geqslant 140$ and < 200 mg/dl.
Results: IGT was detected in 46 of the 173 participants ($\sim 27\%$); no cases of type 2 diabetes were identified. No significant differences were found between youth with NGT and those with IGT in absolute VO_{2max} (2.2 ± 0.6 vs 2.1 ± 0.5 l/min), VO_{2max} adjusted for gender, age, and body composition (2.2 ± 0.2 vs 2.1 ± 0.2 l/min), or recreational physical activity levels (8.7 ± 8.2 vs 6.9 ± 6.2 h/week).
Conclusion: Overweight Hispanic youth with IGT exhibit similar levels of VO_{2max} and physical activity compared to their NGT counterparts. Longitudinal analyses are necessary to determine whether fitness/activity measures contribute significantly to diabetes risk over time in this group.
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Introduction

The prevalence of overweight (BMI$\geqslant$95th percentile) in children has increased dramatically in recent years.[1] More worrisome are the metabolic comorbidities that often accompany a high level of body fat such as impaired glucose tolerance (IGT) and type 2 diabetes. Recent data suggest that nearly 30% of overweight children have IGT.[2–4] In adults, IGT is thought to be an intermediate stage in the pathogenesis of type 2 diabetes.[5] Although the predictive value of IGT in children is yet to be established, cross-sectional evidence indicates that early signs of β-cell insufficiency suggest a higher risk for the development of type 2 diabetes in these youth.[2]

Given that reduced cardiovascular fitness is an early aberration in healthy adults at risk for type 2 diabetes,[6] and high levels of cardiovascular fitness and physical activity are protective against future development of IGT and diabetes,[7,8] it is plausible that fitness and activity are key determinants of IGT in children. To date, the associations between IGT, fitness, and physical activity have not been adequately examined in children. Therefore, the purpose of the present investigation was to compare cardiovascular fitness and physical activity in overweight Hispanic children with normal glucose tolerance (NGT) to those with IGT. We hypothesized that children with IGT would have lower levels of cardiovascular fitness and perform less physical activity compared to children with NGT.

Methods

Sample

The sample comprised 169 children from the University of Southern California (USC) SOLAR (Study of Latino

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Adolescents at Risk) Diabetes Project, an ongoing longitudinal investigation to explore risk factors for the development of type 2 diabetes in at-risk youth. Children were recruited from the greater Los Angeles County through community health clinics, health fairs, and word of mouth. Inclusion criteria: (1) Hispanic ethnicity, (2) age 8–13 years; (3) a family history of type 2 diabetes (sibling, parent, or grandparent), and (4) age and gender BMI$\geqslant$85th percentile based on the standards of the Centers for Disease Control and Prevention. Exclusion criteria: (1) prior major illness, including type 1 or type 2 diabetes (2) medication/condition (e.g., growth hormone, glucocorticoid therapy, hypothyroid, Cushing's disease, Down's syndrome) known to influence body composition, insulin action, or insulin secretion. This study was approved by the USC Institutional Review Board. Written informed consent and assent were obtained from all parents and children prior to any testing procedures. Data from this cohort have been reported previously.[2,9]

Protocol
Children arrived at the USC General Clinical Research Center (GCRC) at approximately 0800 after an overnight fast. A complete medical history and physical examination, including the assessment of maturation according to the criteria of Marshall and Tanner,[10] were performed under the direction of the project pediatrician (MJW). Height using a wall mounted stadiometer and weight using a medical balance beam were measured to the nearest 0.1 cm and 0.1 kg, respectively. For the oral glucose tolerance test, participants ingested 1.75 g of oral glucose solution/kg body weight (to a maximum of 75 g). Blood samples were taken via antecubital vein catheter for measurement of glucose before and 2 h after glucose load. IGT was defined as a 2-h post challenge plasma glucose value $\geqslant$140 and $<$200 mg/dl.[11]

Body composition
Total body composition (fat mass and soft lean tissue mass) was determined by a whole-body dual-energy X-ray absorptiometry (DEXA) scan using a Hologic QDR 4500W (Bedford, MA).

Cardiovascular fitness
Children completed an all-out, progressive, treadmill test to exhaustion as previously described.[12] Respiratory gasses were collected and measured via open circuit spirometry and analyzed on a MedGraphics CardiO_2 combined exercise system (St Paul, MN). Heart rate was measured continuously throughout the test using a Polar Vantage XL heart rate monitor (Port Washington, NY). Criteria for VO_{2max} included the achievement of at least two of the following: a heart rate $\geqslant$195 b.p.m., a respiratory exchange ratio (RER) $>$1.0, and a plateau in oxygen consumption defined as an increase of oxygen uptake $<$2 ml/kg/min with a concomitant increase in workload.

Physical activity
Qualitative and quantitative information regarding recreational physical activity was estimated by the structured activity questionnaire of Kriska *et al.*[13] in a subset of children ($n=131$) who had complete and valid scores. Interviewers read a comprehensive list of sports and activities and had subjects and their parents indicate how much time was spent on each extracurricular activity outside of school during the previous 12-month period. The average number of hours per week of recreational physical activity was subsequently calculated.

Statistics
Group differences in fitness and physical activity between children NGT or IGT were examined using independent sample *t*-tests and analysis of covariance (adjusting for gender, age, height, total fat mass, and soft lean tissue mass). All analyses were performed using SPSS version 11.0 (SPSS Inc., Chicago, IL) with a type I error set at $P<0.05$.

Results

Descriptive physical and metabolic characteristics of NGT and IGT children are presented in Table 1. Groups did not differ in any demographic or anthropometric variable. By definition, NGT children had significant lower 2-h glucose compared to their IGT counterparts ($P<0.001$). Moreover, NGT children had significantly lower 2-h insulin levels compared to children with IGT ($P<0.001$).

Cardiovascular fitness, physical activity, and glucose tolerance
Cardiovascular fitness and physical activity data are presented in Table 2. No significant between-group differences

Table 1 Physical and metabolic characteristics of participants

	NGT (n = 125)	*IGT* (n = 44)	*Total* (n = 169)
Gender (boys/girls)	(69/56)	(22/22)	(91/78)
Age (years)	11.2±1.7	11.4±1.6	11.2±1.7
Height percentile	65.5±26.8	69.9±22.4	149.8±11.1
Weight percentile	96.1±5.2	95.2±7.8	64.4±19.1
BMI percentile	97.3±2.8	96.8±3.4	28.1±5.3
Tanner	2.3±1.4	2.4±1.5	2.3±1.4
Total percent fat (%)	38.8±6.7	38.0±5.4	38.3±6.6
Fasting glucose (mg/dl)	91.1±6.2	92.6±7.8	91.6±6.8
2-h glucose (mg/dl)	119.3±11.0	150.1±8.6*	127.3±17.1
Fasting insulin (μIU/ml)	15.9±9.8	16.7±9.2	15.9±9.6
2-h insulin (μIU/ml)	133.6±115.0	237.0±157.1*	158.1±134.1

Data presented as mean±s.d. *$P<0.001$.

Table 2 Cardiovascular fitness and physical activity characteristics of participants

	NGT (n = *125*)	*IGT* (n = *44*)	*Total* (n = *169*)
VO_{2max} (L/min)	2.2 ± 0.6	2.3 ± 0.6	2.2 ± 0.6
VO_{2max} (ml/kg/min)	34.5 ± 6.8	34.3 ± 6.5	34.7 ± 6.7
VO_{2max} (ml/kg_lean/min)	59.2 ± 6.4	58.2 ± 7.5	59.0 ± 6.6
Maximum heart rate (beat/min)	201 ± 8	201 ± 8	201 ± 8
Maximum RER	1.12 ± 0.07	1.13 ± 0.08	1.12 ± 0.07
Physical activity (h/week)	8.7 ± 8.2 (*n* = 95)	6.9 ± 6.2 (*n* = 36)	8.2 ± 7.8 (*n* = 131)

Data presented as mean ± s.d.

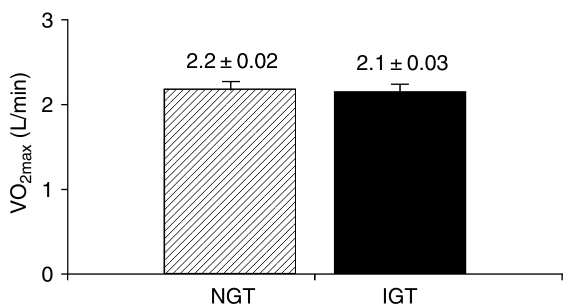

Figure 1 Adjusted least square means of VO_{2max} in children with normal glucose tolerance ▨ vs in paired glucose tolerance ■. Data are mean ± s.e. adjusted for age, gender, height and body composition. *P*-value = 0.17, 95% CI = −0.13–0.01.

were found regarding absolute (l/min) cardiovascular fitness, fitness expressed relative to total body mass (ml/kg/min) or relative to lean tissue mass (ml/kg_lean/min). Similarly, recreational physical activity was not different for children with NGT compared to children with IGT. Figure 1 displays VO_{2max} levels in children with NGT vs IGT adjusted for gender, age, height, and body composition; no significant between group differences were noted.

Discussion

The purpose of the present investigation was to compare cardiovascular fitness and physical activity levels in a sample of overweight Hispanic children with NGT vs IGT. Our results indicated that neither fitness nor activity were significantly different between groups. Although our findings are inconsistent with comparable data from the adult population,[14] prior investigations in children have yielded similar outcomes as the present study in regards to cardiovascular fitness, physical activity, and diabetes risk factors.[9,14] The present study adds to the growing body of literature in the pediatric population examining issues pertaining to fitness, activity, and glucose regulation in high risk youth and is the first investigation to date to compare fitness and/or activity levels between NGT and IGT children.

Fitness and glucose tolerance

In adults, cardiovascular fitness is a key independent determinant of glucose metabolism.[15] Takemura *et al*.[8] found that higher levels of fitness at baseline were protective against the development of IGT over a 20-year period. The protective effect of fitness was evident even after adjusting for baseline and follow-up BMI. Similarly, Wei *et al*.[7] have shown that impairments in glucose regulation are associated with lower fitness levels independent of potential confounders such as adiposity, smoking status, and family history of diabetes. Although the protective effect of fitness on glucose homeostasis in adults is not entirely understood, it may be a reflection of exercise induced alterations in skeletal muscle substrate metabolism.[16] In adults, exercise training results in specific adaptations to skeletal muscle such as increased mitochondrial volume and density and oxidative enzyme capacity which in turn lead to improvements in glucose metabolism as well as increases in VO_{2max}.

It is unclear whether regular exercise (and hence higher fitness levels) leads to similar alterations to the metabolic properties of skeletal muscle of children. While children can improve fitness levels through exercise training[17] the mechanisms by which these improvements take place are largely unknown. Unlike in adults, body composition rather than fitness may be the primary determinant of diabetes risk in the pediatric population.[18] This may explain why we did not find fitness differences between groups in the present study, as NGT and IGT children did not differ in total or regional adiposity (visceral fat data not shown).

Previous studies in children relating to fitness and various measure of diabetes risk have revealed contradictory findings. Some investigations have shown significant independent associations between fitness and glucose metabolism[12] while others have failed to find that fitness is significantly related to diabetes risk.[9,19] These discrepant results may be due to variations in study population and/or methodologies, however, glucose tolerance status was not addressed and thus it is difficult to ascertain whether cardiovascular fitness wields a unique protective effect against this measure of diabetes risk.

Activity and glucose tolerance

Adults who maintain a physically active lifestyle exhibit reduced rates of IGT and type 2 diabetes. It appears that physical activity exerts a protective effect on diabetes through direct and indirect mechanisms. Physical activity directly improves insulin sensitivity through increased skeletal muscle glucose uptake, and indirectly through improvements in body composition.[20] In children, the data are equivocal with regards to physical activity patterns and diabetes risk. Some researchers have reported beneficial associations between activity levels and diabetes risk,[21] while others have not found a significant relationship.[22] As children tend to perform activity in short sporadic bouts, the volume and intensity may be insufficient for the health promoting benefits observed in adults.[23] Given the lack of data compared to the adult population and the differences in methodologies across investigations, it is difficult to come to a definitive conclusion regarding activity and risk profile in youth. Alternatively, a growing body of research has suggested that physical inactivity rather than physical activity may be more important determinant of metabolic health in children.[24] Nonetheless, the current investigation fails to discriminate physical activity differences between children with and without IGT.

Although we did not find group differences in either cardiovascular fitness or physical activity, this is not altogether surprising. The pathogenesis of diabetes normally occurs over a period of decades.[5] Our combined sample was 11.2 years old, Tanner stage ∼2 (i.e. just entering early puberty) and were therefore perhaps very early in the anticipated progression through IGT to type 2 diabetes. When NGT and IGT children were examined together, beta cell function and insulin sensitivity (measure via the frequently sampled intravenous glucose tolerance test and minimal modeling) were significantly and inversely associated with age (data not shown). Collectively, these findings suggest that the metabolic abnormalities observed in diabetic adults, that is, insulin resistance and beta cell failure are more pronounced in the older children. Given these age-associated observations, it is plausible that as children with IGT mature and their disease state progresses, impairments in cardiovascular fitness and/or physical activity may be more evident. Longitudinal analyses are necessary to confirm whether fitness/activity measures contribute significantly to diabetes risk over time in this group of children.

Despite several strengths of our study including: a distinct and well characterized population of at-risk youth, sophisticated quantification of body composition by DEXA, a direct measure of VO_{2max}, and the assessment of glucose tolerance based upon objective clinical criteria, we acknowledge a few noteworthy limitations. First, although our homogeneous population can be considered strong from the perspective of study design, the children in our study were recruited from the greater Los Angeles for their distinct risk profile, therefore; our findings must be taken in this context and are only representative of this subsample of youth. Second, our measure of physical activity was a subjective recall and while we employed procedures to rule out potential outliers, inaccuracies in reporting were possible. Lastly, the crosssectional nature of the study precludes any conclusions regarding the predictive value of fitness and/or activity to diabetes risk.

In conclusion, overweight Hispanic children with IGT do not have lower cardiovascular fitness or physical activity levels compared to their NGT counterparts. It is apparent from the relative paucity of data regarding fitness, activity, and diabetes risk in children that these questions merit further research in this and other at-risk populations of youth. Furthermore, whether changes in fitness and/or activity due to intervention or biological growth are related to favorable/detrimental changes in glucose tolerance warrants further investigation. These studies may provide insight towards the development of appropriate prevention and treatment programs for youth at high-risk for type 2 diabetes.

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