Insulin Sensitivity as an Independent Predictor of Fat Mass Gain in Hispanic Adolescents

TANJA C. ADAM, PHD
CLAUDIA TOLEDO-CORRAL, MS
CHRISTIANNE J. LANE, PHD
MARC J. WEIGENSBERG, MD
DONNA SPRUIJT-METZ, PHD
JAIMIE N. DAVIES, PHD
MICHAEL I. GORAN, PHD

OBJECTIVE — The purpose of this study was to examine the relationship between changes in insulin sensitivity and subsequent changes in fat mass in obese Hispanic children over 3 consecutive years.

RESEARCH DESIGN AND METHODS — In a longitudinal research design, insulin sensitivity (S_i) of 96 research participants was determined at baseline and 1 year later. Body adiposity was assessed at four assessments.

RESULTS — The change in S_i during the first year of the study was a significant predictor of further fat mass development ($P < 0.05$). Considering different directions of S_i change, S_i was a strong predictor for further fat mass development only in the group that decreased their S_i ($P < 0.05$).

CONCLUSIONS — The results show that the direction of change in insulin sensitivity at an early age is an important independent predictor for further fat mass development and emphasize the importance of insulin sensitivity as a primary target for long-term obesity prevention, as well as the significance of early age intervention.

Diabetes Care 32:2114–2115, 2009

Hispanic youth are disproportionately affected by the pediatric obesity epidemic and the associated comorbidities such as type 2 diabetes (1). Although the pathogenesis of type 2 diabetes in children remains unclear, it likely involves characteristics similar to those of adults (2), including the negative effect of increased adiposity on insulin sensitivity and subsequent β-cell failure (3,4). While insulin resistance traditionally has been examined as a consequence of increased adiposity, there is evidence that insulin resistance at an early age in turn may increase adiposity in adolescents and early adulthood (5). The purpose of this study is to further clarify whether changes in insulin resistance early in life are related to fat mass development later in life in Hispanic adolescents.

RESEARCH DESIGN AND METHODS

— The analysis included data from 96 (29 female and 67 male; Tanner stages 1 and 2) overweight (BMI 26.7 ± 4.6 kg/m^2; BMI percentile 96.9 ± 4.1) children who are part of the University of Southern California Study of Latino Adolescents at Risk (USC SOLAR) diabetes project, a longitudinal study that examines the development of type 2 diabetes in at-risk Hispanic youth. The subsample was chosen from a larger cohort ($n = 222$) based on Tanner stage and the completeness of their measures from four consecutive annual visits. Insulin sensitivity, acute insulin response, and disposition index were assessed annually with a frequently sampled intravenous glucose tolerance test (FSIVGTT). The FSIVGTT was performed in the morning after an overnight fast as previously described (6). Body composition was determined annually with a whole-body dual-energy X-ray absorptiometry scan using a Hologic QDR 4500W. Intra-abdominal and subcutaneous abdominal adipose tissue were determined by magnetic resonance imaging using a GE 1.5 Signa LX-Ecospeed with a GE 1.5 Tesla magnet and a single slice at the level of the umbilicus.

Included in the study were healthy children of Hispanic ethnicity and a BMI that was at or above the 85th percentile for age and sex (7).

A detailed description of the methods and the study protocol for the USC SOLAR study have been previously published (8).

Data analysis

Change in S_i for all 96 participants and for the two groups with the different direction of S_i change was determined by subtracting S_i at the first follow-up from baseline S_i. Subsequent changes in fat mass were analyzed as a function of change in S_i over the remaining 2 years using repeated-measures ANCOVA. Whether changes in fat mass determined further S_i development was tested in the same way. All analyses were adjusted for baseline fat mass, fat-free mass at all visits, baseline S_i, change in S_i, age, Tanner stage, and sex.

RESULTS

— S_i decreased significantly over the period of 3 years from 2.4 ± 1.4 ([×10^{-4} min^{-1}/(μU/ml)]^3 at baseline to 1.5 ± 0.79 [(×10^{-4} min^{-1}/(μU/ml)]^3 at the fourth consecutive annual assessment ($P < 0.05$), while fat mass increased from 21.8 ± 8.7 to 28.9 ± 10 kg ($P < 0.05$). For the whole group, the change in S_i during the first study year was a significant predictor of further fat mass development ($P < 0.05$), independent of fat-free mass, change in S_i, age, Tanner stage, and sex. In return, the change in fat mass between baseline and the first follow-up was not related to a change in S_i over the following 2 years.

When comparing a subgroup that significantly increased their S_i during the initial study year ($n = 17$) with a group that

From the Departments of Preventive Medicine, Physiology, Biophysics, and Pediatrics, Keck School of Medicine, University of Southern California, Los Angeles, California.
Corresponding author: Michael I. Goran, goran@usc.edu.
Received 6 May 2009 and accepted 27 July 2009. Published ahead of print at http://care.diabetesjournals.org on 12 August 2009. DOI: 10.2337/dc09-0833.

decreased in S_i ($n = 79$) during that time, the change in S_i was a strong predictor for further fat mass development only in the group that decreased their S_i ($P < 0.05$), not in the group that increased in S_i during the first year. Fat mass increased from 21.3 ± 7.5 to 26.2 ± 10.9 kg in the group that increased in S_i and from 21.9 ± 8.9 to 29.4 ± 9.9 kg in the group that decreased in S_i during the initial study year. Baseline S_i, age, fat mass, lean body mass, and specific fat compartments (intra-abdominal and subcutaneous abdominal adipose tissue) were not different between the two groups.

CONCLUSIONS — The main finding of the analysis is that the first-year change in S_i was an independent predictor of subsequent gain in fat mass over the next 2 years, specifically in those who decreased in S_i. The result was independent of fat-free mass, sex, age, and Tanner stage and is in accordance with a recently published study reporting preteen insulin resistance as a predictor for weight gain (5).

While a decrease in insulin sensitivity traditionally has been looked at as a consequence of increased body adiposity, the present study shows that insulin resistance in turn might also be a cause of increased body adiposity. Hispanic youths are more likely to be insulin resistant than their Caucasian peers, independent of body adiposity (2), predisposing them to an even higher disease risk. We can only speculate on the possible mechanisms behind that relationship, but among other possibilities it very well might involve the effects of insulin resistance on the brain. Insulin receptors have been located in areas that are important for the motivational regulation of food intake (9). Recently, evidence emerged that insulin resistance in the brain might co-occur with insulin resistance in the periphery (10). Sufficient insulin supply, transport, and reception in the brain are thus essential for the maintenance of energy balance. Considering this evidence, the present study might be supportive of the idea that the natural defense against excessive weight gain through adiposity signaling can be undermined by acquired resistance to adiposity-regulating hormones (11,12). The results of the present study show that the change in insulin sensitivity at an early age is an important independent predictor for further weight gain and emphasize the importance of insulin sensitivity as a primary target for long-term obesity prevention in addition to it being a secondary target to weight loss.

Acknowledgments — This study was supported by the National Institutes of Health (R01 DK 59211), the American Diabetes Association (7-05-MN-22), and in part by the General Clinical Research Center, National Center for Research Resources (grant MO1 RR 00043).

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

We thank Courtney Byrd-Williams and Emily Ventura for their help with the manuscript preparation and their contribution to the discussion of the results.

References

1. Forrest KY, Leeds MJ. Prevalence and associated factors of overweight among Mexican-American adolescents. J Am Diet Assoc 2007;107:1797–1800
2. Goran MI, Bergman RN, Cruz ML, Watanabe R. Insulin resistance and associated compensatory responses in African-American and Hispanic children. Diabetes Care 2002;25:2184–2190
3. Boyko EJ, Fujimoto WY, Leonetti DL, Newell-Morris L. Visceral adiposity and risk of type 2 diabetes: a prospective study among Japanese Americans. Diabetes Care 2000;23:465–471
4. Kahn SE. Clinical review 135: The importance of beta-cell failure in the development and progression of type 2 diabetes. J Clin Endocrinol Metab 2001;86:4047–4058
5. Morrison JA, Glueck CJ, Horn PS, Schreiber GB, Wang P. Pre-teen insulin resistance predicts weight gain, impaired fasting glucose, and type 2 diabetes at age 18–19 y: a 10-y prospective study of black and white girls. Am J Clin Nutr 2008;88:778–788
6. Weiss R, Taksali SE, Tamborlane WV, Burgert TS, Savoye M, Caprio S. Predictors of changes in glucose tolerance status in obese youth. Diabetes Care 2005;28:902–909
7. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999–2000. JAMA 2002;288:1728–1732
8. Goran MI, Bergman RN, Avila Q, Watkins M, Ball GD, Shaibi GQ, Weigensberg MJ, Cruz ML. Impaired glucose tolerance and reduced beta-cell function in overweight Latino children with a positive family history for type 2 diabetes. J Clin Endocrinol Metab 2004;89:207–212
9. Figlewicz DP. Adiposity signals and food reward: expanding the CNS roles of insulin and leptin. Am J Physiol Regul Integr Comp Physiol 2003;284:R882–R892
10. Anthony K, Reed LJ, Dunn JT, Bingham E, Hopkins D, Marsden PK, Amiel SA. Attenuation of insulin-evoked responses in brain networks controlling appetite and reward in insulin resistance: the cerebral basis for impaired control of food intake in metabolic syndrome? Diabetes 2006;55:2986–2992
11. El-Haschimi K, Lehnert H. Leptin resistance: or why leptin fails to work in obesity. Exp Clin Endocrinol Diabetes 2003;111:2–7
12. Schwartz MW, Niswender KD. Adiposity signaling and biological defense against weight gain: absence of protection or central hormone resistance? J Clin Endocrinol Metab 2004;89:5889–5897