INSULIN SENSITIVITY AS AN INDEPENDENT PREDICTOR OF FAT MASS GAIN IN HISPANIC ADOLESCENTS

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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 three consecutive years.

Research Design and Methods: In a longitudinal research design insulin sensitivity (SI) of 96 research participants was determined at baseline and 1 year later. Body adiposity was assessed at all four assessments.

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

Conclusions: The results show the direction of change in insulin sensitivity at an early age as 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.

Hispanic youth are disproportionately affected by the pediatric obesity epidemic and the associated co-morbidities such as type 2 diabetes (1). Although the pathogenesis of type 2 diabetes in children remains unclear, it likely involves characteristics similar to that of adults (2), including the negative effect of increased adiposity on insulin sensitivity and subsequent ß-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). Purpose of the present 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.

METHODS AND PROCEDURES

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 USC SOLAR study, a longitudinal study that examines the development of type 2 diabetes in at-risk Hispanic youth. The sub-sample 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 DEXA scan using a Hologic QDR 4500W. Intra-abdominal adipose tissue (IAAT) and subcutaneous abdominal adipose tissue (SAAT) were determined by magnetic resonance imaging (MRI) 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 body mass index that was at or above the 85th percentile for age and gender (7).

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

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

Results are expressed as means (M) ± standard error of the mean (SEM).

RESULTS

SI decreased significantly over the period of three years from 2.4 ± 1.4 [x10^{-4}min^{-1}/(µU/mL)]^3 at baseline to 1.5 ± 0.79 [x10^{-4}min^{-1}/(µU/mL)]^3 at the fourths assessment (p < 0.05), while fat mass increased from 21.8 ± 8.7 kg to 28.9 ± 10 kg (p < 0.05). For the whole group the change in SI during the first study year was a significant predictor of further fat

mass development (p < 0.05), independent of fat free mass, change in SI, age, Tanner stage and gender. In return the change in fat mass between baseline and the first follow up was not related to a change in SI over the following 2 years.

When comparing a sub-group that significantly increased their SI during the initial study year (n = 17) with a group that decreased in SI (n = 79) during that time, the change in SI was a strong predictor for further fat mass development only in the group that decreased their SI (p < 0.05), but not for the group that increased in SI during the first year. Fat mass increased from 21.3 ± 7.5 kg to 26.2 ± 10.9 kg in the group that increased in SI, and from 21.9 ± 8.9 kg to 29.4 ± 9.9 kg in the group that decreased in SI during the initial study year. Baseline SI, age, fat mass, lean body mass and specific fat compartments (SAAT or IAAT) were not different between the two groups.

DISCUSSION

The main finding of the analysis was that initial 1-year change in SI was an independent predictor of subsequent gain in fat mass over the next two years specifically in those who decreased in SI. The result was independent of fat free mass, gender, age and Tanner stage and is in accordance with a recently published study reporting pre-teen 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 possible mechanisms behind that relationship, but amongst other possibilities it very well might involve 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.

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