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Insulin resistance is not associated with thermogenic effect of a high-fat meal in obese children

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ABSTRACT

In adults, insulin resistance may decrease the thermogenic effect of food, contributing to weight gain. We aimed to determine the effect of insulin resistance on energy expenditure in children with long-standing obesity. We hypothesized that thermogenic effect of food would decrease with increasing insulin resistance. Energy expenditure was measured using whole room indirect calorimetry in obese children 7 to 18 years old. Participants were fed a high-fat meal with energy content equal to 35% of measured resting energy expenditure. Thermogenic effect of food was measured for 180 minutes posttest meal and expressed as a percent of calories consumed. Body composition was assessed using whole-body dual-energy x-ray absorptiometry. Fasting glucose, insulin, and hemoglobin A1C were measured. Complete data were available for 25 children (median age, 12.1 years; 52% male). As expected, a significant decrease in resting energy expenditure was observed with increasing Tanner stage ($P = .02$ by Kruskal-Wallis test). Insulin sensitivity, as determined by homeostasis model assessment index equation, did not significantly affect resting energy expenditure ($P = .3$) or thermogenic effect of food ($P = .7$) after adjustment for Tanner stage. In conclusion, our study did not find an association between insulin resistance and energy expenditure in obese children.

1. Introduction

Obesity in children is a growing epidemic in the United States, and up to a third of school-aged children are overweight or obese [1]. Obesity is a multifactorial disease with underlying causes including genetic susceptibility and environmental factors. The thermic effect of food (TEF) is a loss of energy due to the active processing of food and accounts for approximately 10% of the daily energy expenditure [2]. Several studies in adults have shown that obese adults have a decreased TEF compared with nonobese adults, suggesting that obese adults may have a more efficient energy metabolism than normal-weight adults [3,4]. Insulin resistance has been postulated to further decrease TEF in adults, contributing to excess weight gain [3,5].

Past studies have shown that obese children may have a reduced TEF after a high-carbohydrate or high-fat meal when compared with lean controls, but were limited by very small

Abbreviations: BMI, body mass index; HOMA-IR, homeostasis model assessment index equation; REE, resting energy expenditure; TEF, thermic effect of food.

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sample sizes of 6 obese girls [6] and 10 obese boys [7], respectively. It is unknown if insulin resistance further decreases TEF in obese children. Children have difficulty tolerating prolonged measurement of energy expenditure by indirect calorimetry using mouthpieces or hoods; therefore, there are few studies on TEF in obese children. In order to increase patient tolerance of indirect calorimetry, we used a whole-room indirect calorimetry chamber to measure resting energy expenditure (REE) and TEF in children with long-standing obesity. Our objective was to measure TEF in obese, nondiabetic children with varying degrees of insulin resistance. We hypothesized that TEF would decrease with increasing insulin resistance in these children.

2. Methods and materials

2.1. Participants

Thirty-four children between 7 and 18 years old with a history of obesity onset prior to 10 years old (defined as body mass index (BMI) >95th percentile on Centers for Disease Control and Prevention growth charts) were recruited at Vanderbilt University from November 2010 through December 2011, as previously described [8]. Exclusion criteria included diabetes, Cushing syndrome, Prader-Willi syndrome, growth hormone deficiency, and use of metformin or other appetite-altering drug in the past 3 months. Patients with well-controlled hypothyroidism were eligible to participate. Study visits were held at the Clinical Research Center at Vanderbilt University (Nashville, TN, USA). All studies were approved by the institutional review board of Vanderbilt University. Informed consent was obtained from all participants or a parent of the participant, and assent was obtained from participants younger than 18 years.

2.2. Anthropometrics

Standing height was measured using a wall-mounted stadiometer. Weight was measured using a digital scale, lightly clothed and without shoes. Body mass index was calculated using the equation BMI = weight (kg)/height $(m)^2$. Body mass index, height, and weight z scores were also calculated as SDs from the mean using sex- and age-specific Centers for Disease Control and Prevention growth charts (www.cdc.gov/growthcharts/cdc_charts.htm). Fat mass was measured by whole-body dual-energy x-ray absorptiometry using pediatric software (Lunar Prodigy; GE Medical Systems, Madison, WI, USA). Skeletal muscle mass was estimated using appendicular lean tissue mass (A_{LTM}), and organ/viscera tissue mass was estimated using nonappendicular lean tissue mass (NA_{LTM}) [9].

2.3. Laboratory assessment

A fasting blood sample was obtained for measurement of glucose (mg/dL), insulin (μU/mL), and hemoglobin A1C. Insulin resistance was calculated using the homeostasis model assessment index equation (HOMA-IR = insulin * glucose/405) [10]. Patients were categorized as insulin resistant if the HOMA-IR is greater than >2.5 [10].

2.4. Energy expenditure

Participants were asked to maintain their usual diet and abstain from vigorous exercise in the 2 days prior to the study visit. Participants arrived to the Clinical Research Center in the fasting state Energy expenditure was measured using a previously validated whole-room indirect calorimeter. This whole-room indirect calorimeter allows for precise measurement of energy expenditure on a minute-by-minute basis [11]. The accuracy of our room calorimeter for measuring energy expenditure by routine alcohol combustion tests was 99.2% ± 0.5% (mean ± SD) for 24 hours and 98.6% ± 2.1% for 30 minutes [11]. The system detects short-term changes in metabolic rate to 2.7% for 30 minutes and 0.6% for 2 hours of measurement period. The room has precisely controlled temperature and humidity and is equipped with a window to the outside, window to the adjacent room, food pass window, sink, toilet, chair, and multimedia panel that includes TV. Participants were allowed to view movies, read, or use an iPad during the study. Participants rested quietly with minimal movement in a reclining chair for 30 minutes prior to measurement of REE. Measurements were recorded in 1-minute intervals, and REE was calculated over a 30-minute period from rates of oxygen consumption and carbon dioxide production using the Weir equation [12]. The percent predicted REE (measured REE/predicted REE) was calculated using the Molnar formula [13,14]. Postprandial fat oxidation was calculated using the equation $1.695 * VO_2 - 1.701 * VCO_2$[15].

After measurement of REE, participants were given a high-fat test meal (81% fat, 17% carbohydrate, 2% protein), standardized individually to provide 35% of the measured REE. The meal was consumed in less than 30 minutes, and the remaining shake was weighed to determine calories consumed. Participants who consumed less than 80% of the shake were excluded from the analysis. Thermic effect of food was calculated as the postprandial increase in energy expenditure above the REE for 180 minutes, expressed as percent of calories consumed during the test meal. Participants were directly observed by study personnel and asked to remain seated throughout the study. Only data from when participants were seated quietly with minimal movement as recorded minute-by-minute were included in the analysis.

2.5. Data collection

Study data were collected and managed using REDCap electronic data capture tools hosted at Vanderbilt University [16]. REDCap (Research Electronic Data Capture) is a secure, Web-based application designed to support data capture for research studies.

2.6. Statistical analyses

Unless specified otherwise, data are expressed as median (lower quartile, upper quartile), and nonparametric tests were used. Mann-Whitney *U* test was used for continuous variables and Fisher exact test for categorical variables. Differences in percent predicted REE between Tanner stages were assessed using the Kruskal-Wallis test, followed by Mann-Whitney *U* test if overall significance was less than .05. Multivariable