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African genetic admixture is associated with body composition and fat distribution in a cross-sectional study of children

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Abstract

Objective—Although differences in body composition parameters among African American (AA), Hispanic American (HA) and European American (EA) children are well documented, the factors underlying these differences are not completely understood. Environmental and genetic contributors have been evaluated as contributors to observed differences. This study evaluated the extent to which African or European ancestral genetic background influenced body composition and fat distribution in 301 peripubertal AA ($n=107$), HA ($n=79$) and EA ($n=115$) children aged 7–12.

Design—Estimates of African admixture (AFADM) and European admixture (EUADM) were obtained for every subject using 142 ancestry informative DNA markers. Dual energy X-ray absorptiometry and computed tomography scanning were used to determine body composition and abdominal fat distribution, respectively. Multiple regression models were conducted to evaluate the contribution of admixture estimates to body composition and fat distribution.

Results—Greater AFADM was associated with lower fat mass ($P=0.0163$), lower total abdominal adipose tissue ($P=0.0006$), lower intra-abdominal adipose tissue ($P=0.0035$), lower subcutaneous abdominal adipose tissue ($P=0.0115$) and higher bone mineral content (BMC) ($P=0.0253$), after adjusting for socio-economic status, sex, age, height, race/ethnicity and pubertal status. Greater EUADM was associated with lower lean mass (LM) ($P=0.0056$).

Conclusion—These results demonstrate that ancestral genetic background contributes to racial/ethnic differences in body composition above and beyond the effects of racial/ethnic classification and suggest a genetic contribution to total body fat accumulation, abdominal adiposity, LM and BMC.

Keywords

European genetic admixture; race/ethnicity; abdominal adiposity; bone mineral content; lean mass

Introduction

Differences in body composition among African American (AA), European American (EA) and Hispanic American (HA) children have been well documented in the scientific literature.^{1–3} Studies have consistently shown that AA children have greater bone mineral content (BMC) and lean mass (LM) than EA children and HA children.^{4,5} Additionally, EA

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Conflict of interest

The authors declare no conflict of interest.

and HA children accumulate significantly greater amounts of total fat mass (FM) and intra abdominal adipose tissue (IAAT) relative to AA children.^{2,3,6,7} Population differences in adipose accumulation might impact pediatric growth and development, tracking into adulthood⁸ and translating into risk factors for metabolic disorders. It is important, therefore, to identify and investigate factors that may contribute to early differentiation of individuals' body composition and fat distribution.

Genetic and environmental factors have been evaluated as contributors to body composition and energy balance in children. Genetic contributions to pediatric obesity have also been documented in children.^{9–12} Some candidate genes that contribute to obesity among adults, have been identified in pediatric samples¹² and evidence suggest that the contributions of genes may increase obesity risk as age increases.¹³ Scientific research support the role of socioenvironmental factors in pediatric adiposity, particularly by their influence on physical activity and energy-dense food consumption.^{14–18} Evaluation of the influence of genes and environments on pediatric adiposity in children growing up during the obesity epidemic evidence a strong genetic influence despite the exposure to the obesogenic environment.⁹ As the biological integration of populations continues to increase, the extent to which ancestral genetic background influences disease risk and contributes to genetic variability becomes increasingly paramount toward understanding differences in obesity-related outcomes.

Research initiatives have considered ancestral genetic background as an explanation for population differences related to obesity and body composition.^{19–25} Estimates of genetic admixture (ADM) quantify ancestral background using ancestry informative markers that differ in allelic frequency between parental populations who intermated at some historical time, creating new admixed populations. In the United States, the contributions of West African, European and Amerindian parental populations have been significantly associated with body composition parameters in adults.^{20,24,26,27} However, little is known about how ADM affects body composition and fat distribution in children. The aim of this study was to investigate the extent to which individual estimates of African ancestral admixture (AFADM) and European ancestral admixture (EUADM) contribute to body composition and fat distribution in a cross-sectional study of AA, HA and EA children.

Methods

Subjects and design

Three hundred and one AA ($n=107$), HA ($n=79$) and EA ($n=115$) healthy children aged 7–12 years from Birmingham, Alabama, participated in this cross-sectional study. Race/ethnicity was assigned according to parental self-report. A pediatrician determined children's pubertal status according to the criteria of Marshall and Tanner.^{28,29} Children were excluded from the study if they took any medications known to alter body composition, if the girls had started menstruation, or if the children were Tanner stage 4. The majority of the children in the study were of normal weight (<85th percentile for BMI as defined by the CDC at http://www.cdc.gov/healthyweight/assessing/bmi/childrens_BMI/about_childrens_BMI.html). All children and parents gave informed assent and consent, respectively, before participation. The study was approved by the University of Alabama at Birmingham Institutional Review Board for the use of human subjects in research.

Body composition, anthropometrics and fat distribution assessment

Total FM, LM and BMC was assessed by dual-energy X-ray absorptiometry using a GE Lunar Prodigy densitometer (GE LUNAR Radiation Corp., Madison, WI, USA). Subjects were scanned in light clothing, while lying flat on their backs with arms at their sides. Dual

energy X-ray absorptiometry has been found to be highly reliable for body composition assessment in children.^{30–32} Height was measured to the nearest centimeter using a wall-mounted stadiometer and weight was measured on an electronic scale while children wore light clothing.

Computed tomography scanning was used to quantify the distribution of abdominal adipose tissue as total abdominal adipose tissue, IAAT and subcutaneous abdominal adipose tissue (SAAT). A HiLight/Advantage scanner (General Electric, Milwaukee, WI, USA) was used to perform a single slice (5mm) scan of the abdomen at the level of the umbilicus. The scan was analyzed as a cross-sectional area of adipose tissue using Hounsfield units for adipose tissue of –190 to –30. Computed tomography allows for accurate measurements of body fat distribution in children.^{33,34}

Race/ethnicity

Self-reported ‘race/ethnicity’ may not provide an accurate assessment of both the biological and environmental assumptions often associated with the term, making scientific evaluation of population-based differences challenging. Further, race/ethnicity is self-reported and can vary according to generation, historical periods, social dynamics, and as individuals become more admixed. In our analysis, statistical models include race/ethnicity as a control variable for social and cultural characteristics. Although there is multi-colinearity between the admixture variables and race/ethnicity, race/ethnicity measures a social/contextual construct³⁵ whereas ADM measures genetic ancestral background.³⁶ Therefore, these two measures may provide insight into different measurement constructs and should not be used interchangeably.³⁷

Genotyping and determination of ADM

ADM estimates were obtained from genotyping 142 ancestry informative markers across the human genome informative for European, African and Amerindian ancestry. Genotyping for the measures of ADM was performed at Prevention Genetics (<http://www.preventiongenetics.com>) using the melting curve analysis of single nucleotide polymorphism method and agarose gel electrophoresis, as previously described.³⁶ Molecular techniques for the allelic identification and methodology for ADM application have been described elsewhere.²⁶ Information regarding marker sequences, experimental details and parental population allele frequencies has been submitted to dbSNP (<http://www.ncbi.nlm.nih.gov/SNP/>) under the handle PSU-ANTH. Individual admixture estimates were derived using maximum likelihood method, as was previously described.³⁸ The maximum likelihood method estimates the proportion of genetic ancestry for an individual, using a range of proportions from zero to one and identifies the most probable value of admixture based on the observed genotypes.

Socio-economic status

Socio-economic status (SES) was determined according to the Hollingshead four factor index of social status.³⁹ This scale combines the education level and occupational prestige for the number of working parents in each child’s family. Social class scores using this scale range from 8 to 66, with higher values represent a higher SES. SES has been shown to be related to environmental factors, such as physical activity⁴⁰ and diet.^{40,41} Therefore, SES served as a proxy for the environment in the models.

Statistical analysis

For the purpose of descriptive comparisons, ANOVA was used to detect differences in the variables of interest according to racial/ethnic groups. Multiple linear regression models

were used for statistical analysis to evaluate the relationship of ADM with body composition variables. Values of IAAT, SAAT, FM, total abdominal adipose tissue, LM and BMC were log transformed for normality after visual inspection of residuals from the regression equations. Exploratory models were conducted to test for significant contributions of AFADM, EUADM, sex, age, pubertal status, height, race/ethnicity and SES on each body composition variable. The measured value for each ADM component adds to one; therefore to avoid over specification of the statistical models, only European and African admixture were included in the models. AFADM and EUADM were chosen because they have the greatest range of variability among the AA, HA and EA participants in this sample. Data were analyzed using SAS statistical software version 9.1 (SAS Institute, Cary, NC, USA; 2002). Statistical significance was set at $P < 0.05$.

Results

Descriptive statistics for the children by self-reported race/ethnicity are presented in Table 1. AFADM levels ranged from 15 to 100% in children who self-identified as AA, from 0 to 29% in children self-identified as EA and from 0 to 42% in children self-identified as HA. EUADM levels ranged from 0 to 71% in AA, from 47 to 100% in EA and from 3 to 90% in HA children. SES differed among the three groups, with EA having the highest levels and HA having the lowest ($P < 0.05$). HA children had greater FM, percent body fat, BMI percentile, IAAT and SAAT than EA or AA children ($P < 0.05$). When compared with HA or EA children, AA children had greater LM and BMC ($P < 0.05$).

Results for the multiple regression models assessing the contribution of AFADM and EUADM to parameters of body composition and fat distribution are shown in Table 2. AFADM was inversely associated with FM ($P = 0.0163$), total abdominal adipose tissue ($P = 0.0006$), IAAT ($P = 0.0035$), SAAT ($P = 0.0115$) and positively associated with BMC ($P = 0.0253$). Greater EUADM was associated with lower LM ($P = 0.0056$). These associations were independent of SES, age, pubertal status, height, sex, race/ethnicity and total fat (where applicable, see Table 2). Neither self-reported race/ethnicity, nor SES was significantly associated with any fat parameter. BMC was inversely associated with SES.

Discussion

Epidemiological research has demonstrated that there are racial/ethnic differences in body composition and fat distribution in children,²⁻⁷ which provides evidence that population-based differences in body composition parameters start early in the life course.^{3,7,42,43} The question, however, that remains unanswered, is how early genetic and environmental factors influence those obesity-related parameters that account for population differences. Our results suggest that ancestral genetic background exerts an influence on levels of adiposity as early as 7 years of age and that this influence is independent of non-genetic factors. Research conducted among adults has shown that SES attenuates the relationship between admixture and diabetes, but does not eliminate the significant contributions of admixture to diabetes status.⁴⁴ Our results suggest that levels of body fat in early stages of development are controlled by ancestral genetic makeup, an observation that warrants further study and that might result in the development of intervention strategies targeted to individuals of admixed ancestry.

The findings of this investigation also validate previous research showing that AFADM influences obesity-related outcomes among individuals of admixed backgrounds.^{20,25} Although no other studies have examined the relationship between admixture with total fat and LM in children, our team has previously reported associations between ADM with BMC,²² insulin sensitivity²³ and insulin-like growth factor¹⁹ as well as associations between

AFADM and total fat and LM in adults.^{21,25} The association between higher levels of AFADM and lower SAAT, IAAT, and total abdominal adipose tissue is supported by previous research indicating that most of the variability in abdominal adiposity is attributable to genetic influences.⁹ Consistent with a previous study,²⁷ EUADM was inversely associated with LM. Our results, however, suggest that at the early stage of life, EUADM is not predictive of fat accumulation or distribution.

To the extent to which SES serves as a proxy for environmental influences, our analyses indicate that during childhood, the variability in body composition aspects that underlie racial/ethnic disparities is not accounted for by the 'environment'. Although research has documented that higher SES operates as a protective factor for obesity in children from developed countries whereas the reverse trend occurs among developing nations,^{45–48} recent estimates suggest that the effects of SES on obesity are weakening in the United States.⁴⁹ The observation of a weakening SES effect is in concordance with the results and also supports previous work conducted in this cohort documenting that outcomes reflecting the social environment are not associated with body composition measures and do not appear to be salient factors at this early stage of the life course.⁵⁰ The study and understanding of the environmental determinants, their interaction with genetic aspects and their influence on racial/ethnic differences in obesity-related outcomes is an area in need of further research.

Although the findings of this study are important, it is not without limitations. The majority of previous studies on body composition in children have used anthropometrics to examine racial/ethnic differences in fat distribution;⁵¹ hence, our robust measures utilizing dual energy X-ray absorptiometry and computed tomography scans expand on previous findings. Although we accounted for racial/ethnic groups and SES in the models, it is important to stress that race/ethnicity and/or SES variables do not solely account for the extensive cultural and socio-demographic factors that differ by race/ethnicity and could potentially contribute to variation in adiposity levels. Additionally, this study uses a cross-sectional design and the findings will require further verification in a longitudinal analysis.

In summary, the data suggest a role for AFADM and EUADM in the etiology of racial differences in body composition and abdominal fat distribution during childhood. Further investigation is required to identify the specific genes that account for racial/ethnic variation in fat distribution and fat accumulation.

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Table 1

Characteristics of the study population by ethnic group (mean, s.d.)

	EA (n = 115)	AA (n = 107)	HA (n = 79)
Age (years)	9.67 (1.67)	9.55 (1.49)	9.43 (1.59)
Sex (% female)	46.96	45.79	49.37
Tanner stage (% tanner stage 3)	7.89 ^b	23.08 ^a	7.69 ^b
SES (Hollingshead 4-factor index)	49.12 (9.47) ^a	36.51 (11.71) ^b	25.87 (11.67) ^c
BMI percentile	59.71 (26.83) ^b	62.79 (27.26) ^b	79.51 (18.11) ^a
Weight (kg)	35.56 (8.73)	36.72 (9.86)	38.08 (10.09)
Height (cm)	140.21 (10.54)	140.63 (10.45)	137.38 (10.65)
Lean mass (kg)	25.43 (5.0) ^{ab}	26.78 (5.55) ^a	24.77 (5.04) ^b
Fat mass (kg)	8.17 (5.11) ^b	7.69 (5.72) ^b	11.26 (5.83) ^a
Percent body fat	22.22 (8.48) ^b	19.92 (9.09) ^b	28.86 (8.17) ^a
BMC	12.40 (2.72) ^b	13.55 (3.52) ^a	12.50 (2.94) ^b
IAAT (cm ²)	34.28 (22.63) ^b	26.58 (18.56) ^c	42.31 (24.50) ^a
SAAT (cm ²)	85.92 (73.71) ^b	79.73 (80.82) ^b	123.81 (62.91) ^a
TAAT (cm ²)	120.20 (94.12) ^b	106.32 (96.19) ^b	166.12 (83.62) ^a
Percent European admixture	96.19 (3.71) ^a	16.28 (14.91) ^c	37.77 (17.97) ^b
Percent African admixture	0.56 (1.35) ^c	79.04 (15.48) ^a	6.39 (8.14) ^b
Percent Amerindian admixture	3.24 (3.47) ^b	4.68 (4.12) ^b	55.84 (19.17) ^a

Abbreviations: BMC, bone mineral content; BMI percentile, body mass index percentile; IAAT, intra abdominal adipose tissue; SAAT, subcutaneous abdominal adipose tissue; SES, socioeconomic status; TAAT, total abdominal adipose tissue.

^{a,b,c} Indicate significant differences between the groups with an alpha level of <0.05.

Table 2

Multiple linear regression results for the association of African and European admixture with body composition and fat distribution

Total sample (<i>n</i> = 301)	African genetic admixture estimate		European genetic admixture estimate	
Fat mass	−0.48	0.0163*	0.06	0.8312
Total abdominal adipose tissue	−0.33	0.0006*	−0.15	0.2275
Subcutaneous abdominal adipose tissue	−0.42	0.0115*	−0.08	0.7193
Intra abdominal adipose tissue	−0.57	0.0035*	−0.34	0.1949
Bone mineral content	0.11	0.0253*	0.08	0.2293
Lean mass	−0.04	0.1996	−0.13	0.0056*

All models have been adjusted by sex, age, socio-economic status, height, ethnicity and pubertal status. The models for intra abdominal adipose tissue, subcutaneous abdominal adipose tissue and total abdominal adipose tissue have also been adjusted for total fat. The model for fat mass was adjusted by lean mass. Significance of alpha <0.05 is shown in bold with an asterisk.