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*Original Research Article*

# The Relationship Between European Genetic Admixture and Body Composition Among Hispanics and Native Americans

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*ABSTRACT* Previous studies have shown a relationship between health-related phenotypes and the degree of African, European, or Native American genetic admixture, indicating that there may be a genetic component to these phenotypes. However, these relationships may be driven to a large extent by the environmental differences that co-vary with admixture differences between and within groups. In this study, we examine the relationship between genetic admixture and two phenotypic measurements that are potentially related to health: body mass index (BMI) and percent body fat (PBF). In addition to admixture proportions, we attempt to assess the influence of some environmental covariates by examining how the phenotypes vary with self-reported household income, education of parents, and physical activity level. Genetic, anthropometric, and environmental data were collected from 170 self-reported Hispanic and Native American university students in Albuquerque, NM. We examine the relationships between genetic admixture, phenotype, and environment in both the full sample, as well as in Hispanics and Native Americans separately. Among Hispanics, we find no significant relationship between genetic admixture and body composition. Among Native Americans, despite a small sample size, we find a statistically significant, negative relationship between European genetic admixture and PBF and BMI, after adjusting for other predictor variables. We compare our findings to previous research, and discuss their implications for understanding health disparities within and between ethnic groups. Am. J. Hum. Biol. 21:377–382, 2009. 

It is difficult to determine the extent to which differences in health-related phenotypes between various US ethnic groups are driven by the genetic differences between those groups, because genetic and environmental differences tend to co-vary (Burchard et al., 2003; Foster and Sharp, 2002; Gravlee and Dressler, 2005; Paradies et al., 2007; Risch, 2006). From a medical genetics perspective, it is important to elucidate the effects of both genetic and environmental factors on health (Foster and Sharp, 2002; Sankar, 2006). It may also be important to determine the potential for stratification bias in association studies (Gonzalez Burchard et al., 2005; Tang et al., 2006) due to the heterogeneity in admixture proportions in groups such as Hispanics who can show anywhere between 0 and 90% Native American (NA) admixture (Bertoni et al., 2003; Bonilla et al., 2004a; Gonzalez Burchard et al., 2005).

One way to examine the influence of genetic factors on health-related phenotypes that differ between ethnic groups is to look at how those phenotypes vary along a spectrum of individual genetic admixture levels in socially defined ethnic groups such as Hispanics, African Americans, and Native Americans. Using admixed groups such as Hispanics or African Americans who each share a single socially defined group identity yet have heterogeneous admixture proportions can help to attenuate confounding due to environmental factors (Risch et al., 2002; Tang et al., 2006). However, it has been shown that within Hispanics, for example, there are sub-divisions that can potentially have environmental, genetic, and health relevance (Chakraborty et al., 1986; Klimentidis et al., 2008; Lara et al., 2005; Montalvo and Codina, 2001; Sweeney et al., 2007). This makes it difficult to elucidate whether there is an influence of genetic differences between groups on health related phenotypes, and consequently, on disparities in disease risks (Gonzalez Burchard et al., 2005; Halder and Shriver, 2003). To date, several such studies have examined the relative effects of Native American, European, and African genetic admixture on a variety of health-related phenotypes, including hypertension (Reiner et al., 2007; Tang et al., 2006), lung capacity (Brutsaert et al., 2004), bone mineral density (Bonilla et al., 2004b), BMI (body mass index) (Fernandez et al., 2003), asthma (Salari et al., 2005), and diabetes and insulin-related phenotypes (Gower et al., 2003; Hanis et al., 1986; Parra et al., 2004). Many of these studies fail to adequately control for the various possible environmental influences on health (Paradies et al., 2007), making it difficult to make any solid conclusions about the role of genetic differences in health disparities.

Obesity is a major contributor to the onset of type-2 diabetes and metabolic syndrome and is responsible for a large proportion of the overall mortality in the US population. Studies have shown that the risk of developing type-2 diabetes and metabolic syndrome in populations of European descent is lower than it is among Hispanics and Native Americans (Burrows et al., 2000; Cook et al., 2003; Ford et al., 2002; Permutt et al., 2005). Its prevalence is at

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least twice as high in Native American populations as it is in populations of European descent (American Diabetes Association). One previous study found a negative relationship between degree of European genetic admixture and type-2 diabetes among a sample of Native Americans (Williams et al., 2000). However, among Hispanics, this relationship has been difficult to establish (Martinez-Marignac et al., 2007; Parra et al., 2004). Because obesity is a major risk factor for developing type-2 diabetes, as well as other diseases, several studies have attempted to resolve the relationship between genetic admixture and obesity-related traits. These studies frequently measure obesity using BMI, which is a measure of the weight of a person scaled according to height. To our knowledge, there is only one other study that has directly examined the relationship between BMI and genetic admixture among self-identified Native Americans (Williams et al., 2000). In this study of Pima Indians in Arizona, Williams and colleagues found a negative relationship between BMI and European genetic admixture. To our knowledge, there are five previous studies that have examined this relationship among self-identified Hispanics (Bonilla et al., 2004b; Parra et al., 2004; Sweeney et al., 2007; Tang et al., 2006; Ziv et al., 2006). Neither Parra et al. (2004) nor Bonilla et al. (2004b) found a significant relationship between BMI and genetic admixture among Hispanic Americans from the San Luis Valley in southern Colorado and Puerto Rican women from New York City, respectively. Sweeney et al. (2007) found a significant negative relationship between European admixture and BMI among Hispanics in the Southwest US. Similarly, Ziv et al.(2006) found a significant positive relationship between Indigenous American admixture and BMI, but only among foreign-born Latina women in the San Francisco Bay area. In contrast, Tang et al. (2006) found a statistically significant positive relationship between the degree of European admixture and BMI in a sample of Mexican Americans, a result that is potentially inconsistent with the findings of Williams et al. (2000) and Sweeney et al. (2007). The absence of a consistent pattern among these studies, as well as the findings by Martinez-Merignac et al. (2007) of a positive association between socioeconomic status and European genetic admixture suggest that the degree of genetic vs. environmental contribution to health-related phenotypes is still unclear among Hispanics and Native Americans, and thus warrants further investigation.

In this study, we examine the relationship between genetic admixture, environmental factors, and BMI and PBF (percentage body fat) among a sample of self-identified Hispanics and Native Americans in New Mexico. The environmental measures are self-reported activity level, household income, and education levels of subjects' parents. These measures were chosen because they are known to affect obesity (Shrewsbury and Wardle, 2008). We hypothesize that BMI and PBF will decrease with proportional European genetic admixture, independent of the influence of environmental factors.

## METHODS AND PROCEDURES

### *Study population*

We recruited 170 male ($n$ = 59) and female ($n$ = 111) Hispanics ($n$ = 147), Native Americans ($n$ = 15), and mixed ethnicity ($n$ = 8) students from introductory Psychology courses at the University of New Mexico in Albuquerque. Of the self-identified Hispanics in this sample, 78% were born in New Mexico and 95% did at least one-third of their primary schooling in New Mexico. Among self-identified Native Americans, 87% were born in New Mexico and 100% did at least one-third of their primary schooling in New Mexico. The students ranged in ages from 18 to 22. The study recruitment message stated that only Hispanics and Native Americans could participate. Participants were asked to check a box on a questionnaire indicating whether they consider their ethnicity to be White, Hispanic, Native American, or Other. All participants gave written informed consent, and the study was approved by the University of New Mexico Human Research Review Committee.

### *Ancestry informative markers (AIMs)*

Cheek swabs were collected from 185 participants. DNA was extracted from the swabs and purified using established protocols, and a panel of 76 biallelic AIMs was typed (see Supporting Information Table 1). The AIMs are described elsewhere (Bonilla et al., 2004a,b; Choudhry et al., 2006; Martinez-Marignac et al., 2007), and were chosen because they exhibit large allele frequency differences (denoted "δ," where δ = |freq of "A" allele in population 1 − frequency of "A" allele in population 2|) between three major continental population groups: Europeans, West Africans, and Native Americans (see next section for more detail). Average population pairwise δ for these markers are 0.47 between Europeans and West Africans, 0.44 between Europeans and Native Americans, and 0.53 between Native Americans and West Africans. Of 185 initially recruited subjects, 14 were eliminated from further analysis because 50 or fewer AIMs were successfully genotyped, and one was eliminated for self-identifying as "White," leaving a final sample size of 170 subjects.

### *Parental populations*

To assess the genetic ancestry from each of the three parental populations, genotype frequencies were obtained from: (1) 72 individuals of Spanish origin, from the province of Valencia, Spain; (2) 177 individuals from the Native American Cheyenne, Pima, Pueblo and Maya; (3) 279 individuals from the Central African Republic, Nigeria, and Sierra Leone. Continental average allele frequencies from these samples for the 76 AIMs are presented in Supporting Information Table 1. We assume that the parental allele frequencies have not changed significantly due to drift, gene flow, or selection over the last few hundred years (Long, 1991; Wang, 2003). Recent factors, such as disease and a resulting reduction in population size, especially among Native Americans, may have changed these allele frequencies, such that the frequencies observed today do not accurately reflect those of 400 years ago, at the time of initial admixture. Finally, gene flow within the Americas and within Europe (i.e., from other groups in the region) may have affected the allele frequencies over the past 400 years. However, in the case of Native Americans, studies have shown that the allele frequencies of the AIMs like those used in this study do not tend to differ substantially across current-day populations of the Americas (Bonilla et al., 2004a; Luizon et al., 2008).

### *Genetic admixture estimates*

Individual genetic admixture levels were calculated using the maximum likelihood estimation (MLE)

*TABLE 1. Admixture proportions and obesity variables by self-identified ethnicity*

| | N | Native American admixture (%)* | European admixture (%)* | African admixture (%) | BMI (kg/m$^2$) | PBF (%) | Income ($US)* | Education (years) | Activity level |
|---|---|---|---|---|---|---|---|---|---|
| Hispanics | 147 | 32.7 ± 12.4 | 61.6 ± 12.4 | 5.7 ± 6.0 | 24.0 ± 4.3 | 24.8 ± 8.3 | 59,234 ± 32,289 | 14.38 ± 2.64 | 2.18 ± 0.63 |
| Native Americans | 15 | 71.8 ± 18.6 | 25.3 ± 19.1 | 2.9 ± 3.6 | 25.0 ± 3.6 | 28.1 ± 9.2 | 39,792 ± 25,837 | 13.92 ± 1.42 | 2.00 ± 0.68 |

* Represents significant difference, with $P < .05$, between Hispanics and Native Americans.

approach described by Hanis et al. (1986). Given ancestral allele frequencies at a locus, the probability of observing a marker genotype is computed for each locus. The logs of the individual locus probabilities at all loci are then summed. For every possible admixture proportion from 0 to 100, the probability of the observed genotype is computed. The admixture proportion that corresponds to the maximum combined probability across all loci is the one that is the maximum likelihood estimate of ancestry for that individual (Halder, 2005). Other statistical methods used to estimate individual admixture (e.g., STRUCTURE and ADMIXMAP), typically show high degrees of correlation with the MLE method (Bonilla et al., 2004a; Martinez-Marignac et al., 2007).

### *BMI and PBF measures*

Weight and body fat percentage measurements were obtained from a Tanita (Arlington Heights, Illinois) BF681 digital scale, which uses a bioelectrical impedance method to estimate body fat percentage. Weight was rounded to the nearest 0.2 lbs. Height measurements were taken to the nearest 0.25 inch using a measuring tape affixed to a wall. Height and weight were subsequently converted to meters and kilograms. BMI was calculated as weight (kg) divided by height squared (m$^2$). BMI and PBF are likely to be correlated, partly because the scale uses the height and weight information of each individual to determine PBF.

### *Income, education, and activity level*

Environmental variables were assessed through a questionnaire, in which subjects were asked to indicate from a list of ranges the household income of their parents, and the education level of each of their parents. Education was coded as a continuous variable, defined as the number of years of schooling completed. The education level of the mother and father were averaged. Activity levels were assessed while obtaining body fat measurements. Subjects were verbally asked if they were "not active at all," "somewhat active," or "very active." This information was entered into the Tanita scale.

### *Statistical analyses*

To test for differences in average BMI and PBF, and income between Hispanics and Native Americans, Mann Whitney U tests were performed. In subsequent analyses, BMI was transformed to 1/BMI to improve the linearity of the association between BMI and European genetic admixture (Bonilla et al., 2004b; Fernandez et al., 2003; Gonzalez Burchard et al., 2005). No transformation was necessary for PBF. We used univariate GLM with sex as a fixed factor to examine the relationship between the quantitative traits and EU genetic admixture, separately for self-identified Hispanics, and self-identified Native Americans, and for the whole sample. Relationships between quantitative traits (BMI and PBF) and bio-demographic predictor variables (genetic admixture estimates, parental income, parental education, activity level) were assessed by multiple linear regression by use of the statistical package SPSS 12.0. Parental income was coded as income per year, and parental education was coded as the average number of years of education completed by mother and father.

## RESULTS

### *Descriptive statistics*

We find no significant difference between self-identified Native Americans and Hispanics for mean BMI and PBF, parental education level, and activity level (see Table 1). We find a significant difference between the mean income of Hispanics ($59,234) and Native Americans ($39,792) ($P = 0.032$). In addition, Hispanics showed higher variance in education ($P = 0.018$—Levene's test for equality of variances).

We find that males have a significantly lower mean BMI ($P = 0.013$) and PBF ($P < 0.001$) than females. For this reason, we adjust for sex in all the subsequent regression analyses.

### *BMI and genetic admixture*

Among all subjects, BMI (analyzed as 1/BMI) is negatively correlated with EU admixture when all subjects are analyzed ($r^2 = 0.076$, $P = 0.008$, adjusted for sex; see Fig. 1). Persons in the sample with low BMI, therefore, have higher levels of EU ancestry than do persons with high BMI. When self-identified Hispanics ($n = 147$) are analyzed separately, the relationship is not statistically significant ($r^2 = 0.087$, $P$-value = 0.140). When self-identified Native Americans ($n = 15$) are analyzed separately, the relations is significant ($r^2 = 0.683$, $P < 0.001$).

### *PBF and genetic admixture*

We find that 1/BMI and PBF are highly correlated ($r^2 = 0.84$, $P < 0.001$, adjusted for sex). Among all subjects, we find a significant negative relationship between EU genetic admixture and PBF ($r^2 = 0.242$, $P = 0.013$, adjusted for sex; see Fig. 2). Persons in the sample with low PBF, therefore, have higher levels of EU ancestry than do persons with high PBF. When only Hispanics are considered, the relationship is not statistically significant ($r^2 = 0.157$, $P = 0.258$). Among self-identified Native Americans, we find a highly significant relationship between NA admixture and PBF ($r^2 = 0.891$, $P = 0.003$).

### *The influence of other predictor variables*

Multiple linear regression analyses including all predictor variables were performed for the combined sample, then for Hispanics and Native Americans separately

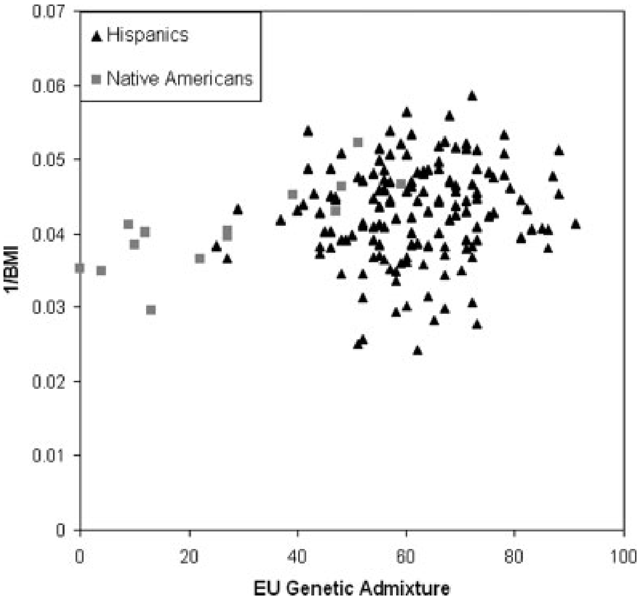


Fig. 1. 1/BMI and European genetic admixture by ethnicity.

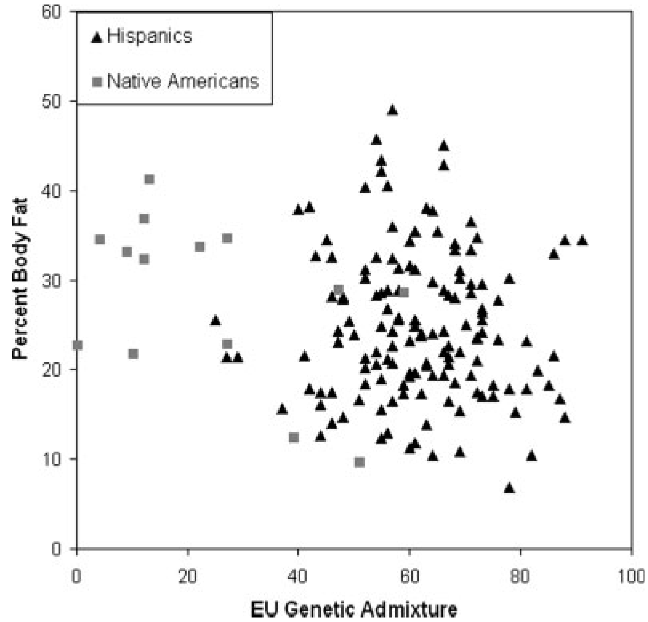


Fig. 2. PBF and European genetic admixture by ethnicity.

(Table 2). The multiple regression for the combined sample shows that sex and EU genetic admixture are the only statistically significant predictors of BMI ($P = 0.041$ and 0.043, respectively). For the Hispanic sample alone, sex is the only significant predictor of BMI ($P = 0.014$). For the Native American sample alone, EU genetic admixture is a highly significant predictor of BMI ($P = 0.005$). We find a similar pattern across groups for PBF.

### SES variables and genetic admixture

Among all subjects, family income ($r^2 = 0.035$, $P = 0.027$), but not average parent education ($P = 0.197$), is positively associated with EU genetic admixture. Among only self-identified Hispanics, family income is positively associated ($r^2 = 0.037$, $P = 0.034$) with EU genetic admixture, but not the average parent education ($P = 0.399$). Among self-identified Native Americans alone, neither family income ($P = 0.241$) nor average parental education ($P = 0.438$) are significantly associated with EU genetic admixture.

## DISCUSSION

We find that across our combined sample of self-identified Native Americans and Hispanics, obesity related traits are better predicted by European genetic admixture than by household income, parental education, or activity level. We find that this relationship is driven to a large extent by the strength of this relationship in the Native American sample. Among Hispanics, we find no evidence of any relationship between EU genetic admixture and any of the obesity-related traits. However, it should be noted that the lower standard deviation in EU genetic admixture in the Hispanic sample (12.4) when compared with the Native American sample (19.1) could have limited our ability to detect a relationship among Hispanics between the obesity-related variables and EU genetic admixture. In addition, it should be noted that our findings among Native Americans should be taken with some degree of reservation due to the small sample size.

These results are interesting in light of Tang et al.'s (2006) results which suggest that the effect of genetic admixture may differ across the admixture spectrum. Specifically, based on their results, Tang et al. find a curvilinear relationship between genetic admixture and BMI, in which BMI decreases with European genetic admixture in the range of 60%–40% European admixture, and increases in the rest of the range. Our results, although only suggestive because of the small sample size, are similar in that BMI appears to slightly decrease from 60% to 40% European admixture, unlike the trend over the rest of the admixture range (data not shown). Unlike Tang et al. who find an unexpected positive relationship between European genetic admixture and BMI, we find no significant relationship among our sample of Hispanics. One possible interpretation for the lack of a straightforward relationship between genetic admixture and BMI and PBF found in this and previous studies is that the environmental component that contributes to variation in BMI and PBF is more heterogeneous among Hispanics than among Native Americans (Bates et al., 2008; Ziv et al., 2006). A dampening of the genetic influence may occur if there is a higher degree of variance in the residual confounds, such as diet, among Hispanics, when compared with Native Americans.

The differences that we observe between populations for the relationship between admixture and phenotype may also be due to the effect of differing admixture histories. If admixture is recent, and the number of loci contributing to the trait is small, then the correlation between genome-wide estimates of admixture and the trait is expected to be higher than if the admixture occurred many generations ago (Tang et al., 2006). It may be that most of the admixture among Hispanics in New Mexico occurred many generations ago, whereas among Native Americans, much of the admixture may have happened more recently.

*TABLE 2. Multiple regression analyses with 1/BMI as the outcome variable using all predictors*

| | Combined sample | | | | Hispanics only | | | | Native Americans only | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Unstand. β | SE | Stand. β | *P* | Unstand. β | SE | Stand. β | *P* | Unstand. β | SE | Stand. β | *P* |
| Sex | −0.003 | 0.001 | −0.201 | 0.041* | −0.004 | 0.001 | −0.265 | 0.014* | 0.002 | 0.003 | 0.189 | 0.500 |
| EU admixture | 0.000 | 0.000 | 0.198 | 0.043* | 0.000 | 0.000 | 0.117 | 0.273 | 0.000 | 0.000 | 0.994 | 0.005* |
| Parental income | 0.000 | 0.000 | −0.001 | 0.990 | 0.000 | 0.000 | 0.001 | 0.993 | 0.000 | 0.000 | 0.235 | 0.288 |
| Parental education | 0.000 | 0.000 | 0.052 | 0.593 | 0.000 | 0.000 | 0.056 | 0.601 | −0.001 | 0.001 | −0.316 | 0.165 |
| Activity level | 0.001 | 0.001 | 0.068 | 0.497 | 0.000 | 0.001 | 0.021 | 0.847 | 0.001 | 0.002 | 0.105 | 0.706 |

The analysis was done for all subjects, then separately by ethnic group.
*Denotes *P*-values less than 0.05. Unstandardized beta coefficients for EU admixture are $7.7 \times 10^{-5}$, $6.3 \times 10^{-5}$, $2.9 \times 10^{-4}$, respectively for the combined sample, Hispanics only, and Native Americans only.

This would result in the pattern between admixture and the phenotypes that we see in this study.

It is also important to highlight that there has been a similar difficulty in establishing a consistent relationship between genetic admixture and BMI among African Americans. Some studies find a positive relationship between African genetic admixture and BMI (Fernandez et al., 2003; Tang et al., 2006), whereas others find no relationship (Reiner et al., 2007).

We found no relationship between either parental socioeconomic variables or activity level and BMI or PBF. The environmental contribution to these obesity-related traits may have larger variation than the genetic admixture contribution, making it difficult to obtain a statistically significant relationship between the environmental variables and the obesity-related traits. Also, because this is a sample taken from university students, individuals of higher SES are likely over-represented, making it more difficult to detect a relationship between SES and obesity. In addition, the subjects in this sample may be too young for there to have been an effect of environmental factors on obesity. The operationalization of these variables also presents several problems that could limit our ability to find relationships between them and our obesity-related variables. First, these measures were self-reported, and subjects reported the income and education level of their parents, because all subjects were young (ages 18–22), and in the educational system. Second, the physical activity measure relies on self-reports and is based on a limited range of variation. However, even when comparing between the most active and the least active individuals, we find no significant difference in average BMI or PBF. Finally, another limitation of this study is that we do not consider variation in dietary intake, which is likely to be one of the most important risk factors for developing obesity. If dietary intake and EU genetic admixture are correlated, any correlation between EU genetic admixture and obesity may simply be due to differences in dietary intake.

## CONCLUSION

Despite our modest sample, we were able to confirm results from previous studies that showed a variable relationship between genetic admixture and obesity-related traits between ethnic groups whose ancestry lies along a European–Native American axis. We also find that neither physical activity level nor parental income or education reliably explain the variation in adiposity. Based on these results, we can not reject the hypothesis that genetic differences between groups are partly responsible for the differences in obesity-related traits. In the future, it will be important to both identify and examine all possible environmental influences, and study these in combination with individual genetic admixture measurements. This will allow us to better understand the complete etiology of disease and health disparities between ethnic groups.

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