Heritabilities of Lipids in Young European American and African American Twins

Anastasia Iliadou,[1] Harold Snieder,[2,3] Xiaoling Wang,[2] Frank A. Treiber,[2] and Catherine L. Davis[2]

[1] *Clinical Epidemiology Unit, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden*
[2] *Georgia Prevention Institute, Department of Pediatrics, Medical College of Georgia, Augusta Georgia, United States of America*
[3] *Twin Research and Genetic Epidemiology Unit, St. Thomas' Hospital, London, United Kingdom*

Twin studies of lipids have almost exclusively involved Caucasians. People of African descent are known to show a healthier lipid profile, but relatively little is known about ethnic differences in genetic and environmental influences on lipids. One hundred and six African American (AA) and 106 European American (EA) twins (30 singletons and 91 complete pairs: 49 monozygotic, 21 dizygotic and 21 opposite-sex) from the south-eastern United States were studied (mean age 17.9 ± 3.2 years; 79% fasting). Lipids were assayed with the Cholestech LDX system. Analyses were adjusted for fasting status. Generalized estimating equations were used to test for the effects of sex and ethnicity on means, controlling for the dependence within twin pairs. Structural equation modeling was used to estimate genetic and environmental effects on each lipid variable. Females showed higher high-density lipoprotein (HDL) values than males ($p < .001$) and AAs showed higher HDL values than EAs ($p < .001$). EA males had higher triglyceride values than other groups ($p = .02$). All parameter estimates could be set equal across sex. Parameter estimates for total cholesterol, triglycerides and HDL could be set equal across ethnicity. The best fitting model for low-density lipoprotein (LDL) showed higher heritability in AAs (.92) than EAs (.69). Heritabilities ranged from 69% to 92%, with remaining variation explained by nonshared environmental effects. Adjustment for body mass index had virtually no effect on the heritability estimates. In this first twin study on lipids to include AAs, no ethnic differences in heritability were found except for LDL, where AAs exhibited higher estimates.

Although great efforts have been expended to improve treatment and prevention, coronary heart disease (CHD) remains one of the most important killers in the western world. African Americans (AAs) are at higher risk for CHD mortality than European Americans (EAs; Clark et al., 2001). As there is compelling evidence that CHD originates in childhood, it is essential to study predictors of CHD at an early age and investigate ethnic differences (Berenson et al., 1992).

Total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglyceride levels are recognized along with obesity as independent risk factors for coronary heart disease (Expert Panel, 2001). For some of these, remarkable ethnic differences have been found. Total cholesterol and LDL in AAs and EAs tend to be similar, but AAs have higher HDL and lower triglycerides than EAs (Gillum, 1999). Longitudinal studies show that ethnic differences in lipid profile are already present in childhood (Srinivasan et al., 1991). Atherosclerosis in childhood has been linked to lipid profile (Berenson et al., 1992). These early ethnic differences in lipid levels may confer a protective effect in AAs on CHD rates in adulthood, as observed in Afro-Caribbeans and West Africans (Whitty et al., 1999). It is currently unclear how the healthier lipid profile in AAs can be reconciled with the higher CHD mortality among AAs (Clark et al., 2001).

The importance of genetic factors explaining individual differences in lipid levels has been established in twin and family studies (Beekman et al., 2002; Iliadou et al., 2001; Iselius, 1979; Snieder et al., 1997). Heritabilities of lipids have been estimated between 50% and 80% for total cholesterol, LDL, HDL and triglycerides, but twin and family studies have almost exclusively involved Caucasians (Snieder et al., 1999). As a consequence relatively little is known about potential ethnic differences in genetic and environmental influences on lipids.

The major aim of our study was, therefore, to estimate and compare the relative influence of genetic and environmental factors on variation in total cholesterol, HDL, LDL and triglycerides, in a sample of young AA and EA twins from the south-eastern United States. We further investigated sex differences and the extent to which heritable influences on lipids are dependent on obesity, an important covariate of lipids that may explain part of its familial aggregation.

Received 28 April, 2005; accepted 20 July, 2005.

Address for correspondence: Catherine L. Davis, PhD, Georgia Prevention Institute, Dept. of Pediatrics, Medical College of Georgia, 1499 Walton Way (HS-1640), Augusta, Georgia 30912, USA. E-mail: cadavis@mcg.edu

https://doi.org/10.1375/twin.8.5.492 Published online by Cambridge University Press

Materials and Methods

Subjects

The sample consisted of 212 twins (mean age: 18 ± 3.2 years), 108 boys and 104 girls (24 monozygotic [MZ], 10 dizygotic [DZ], 12 opposite-sex [OS] twin pairs and 14 singleton EA twins; 25 MZ, 11 DZ, 9 OS twin pairs and 16 singleton AA twins). Zygosity was determined using five standard microsatellite markers in DNA collected with buccal swabs (Jackson et al., 2001). Recruitment of twin pairs into the Georgia Cardiovascular Twin Study has been described previously (Snieder & Treiber, 2002).

Subjects were classified as AA if (1) both parents reported being of African heritage; (2) they and the child were born and raised in the United States; and (3) parents considered themselves and their child to be AA. Subjects were classified as EA if (1) both parents reported that they were of European ancestry; (2) they and the child were born and raised in the United States; and (3) they considered themselves and their child to be EA and not of Hispanic, Native American or Asian descent. All subjects were healthy based on parental report of the child's medical history.

None of the subjects used any lipid lowering medication. The Institutional Review Board at the Medical College of Georgia gave approval for the study. Informed consent was provided by all subjects and by parents if subjects were less than 18 years of age.

Plasma Lipid Measures

The Cholestech LDX system (Cholestech, Hayward, CA) was used to measure levels of total cholesterol, HDL, and triglycerides from frozen plasma. The majority of twins were examined in the morning and fasted overnight (79%). Twins coming on afternoon visits were not required to fast. Fasting status was defined as *yes* (8 hours or more) or *no* (less than 8 hours). LDL levels were calculated by the LDX system (Friedewald et al., 1972). Product literature indicates that between 95% and 98% of LDX values for total cholesterol, HDL, and triglycerides were in complete agreement with the reference method according to the National Cholesterol Education Program criteria, and coefficients of variation (CVs) for the LDX lipid profile tests were 2% to 3% for total cholesterol, 3% to 6% for HDL and 2% to 4% for triglycerides (Cholestech Corporation, 2001). With respect to the current study, the interassay CVs for total cholesterol, HDL and triglycerides were 3.7% to 4.9%, 4.0% to 6.6% and 3.7 to 4.6%, respectively. One limitation of this method is that it only gives results within a certain measurement range. The range for total cholesterol is 2.59 to 12.93 mmol/L (100 to 500 mg/dL). For HDL and triglycerides, the measurement range is 0.39 to 2.59 mmol/L (15 to 100 mg/dL) and 0.51 to 6.77 mmol/L (45 to 600 mg/dL), respectively. Eight individuals for triglycerides, two for total cholesterol and one for HDL had values below the detection limits of the assays and were assigned a value of 0.50 mmol/l for triglycerides, 2.58 mmol/l for cholesterol and 0.38 mmol/l for HDL. Two individuals with HDL values above the detection limit were assigned a value of 2.60 mmol/l.

Statistical Methods

The distributions of lipid values were skewed and therefore transformed by a natural logarithm for total cholesterol and triglycerides and square root for HDL and LDL prior to statistical analysis. Eight lipid measurements were excluded for analyses, because they were considered outliers (greater than 3 *SD*). Analyses of lipid values included descriptive statistics and quantitative genetic analyses.

Descriptive Statistics

Multiple regression was used to test for sex and ethnic differences as well as their potential interaction on the mean lipid levels, and included fasting status, age and body mass index (BMI, weight/height^2) as covariates. Generalized estimating equations (GEE) were used which control for relatedness between twins and that yield unbiased p values.

Quantitative Genetic Analyses

The main aim of our analysis was to estimate the relative influence of genetic and environmental factors on individual differences in each of the lipids and to test for their dependency on ethnicity and sex. The influence of BMI on models was assessed.

A series of univariate models were fitted in five sex-by-zygosity groups (MZ and DZ same-sex and DZ opposite-sex) separately in AAs and EAs in order to test for sex differences. They were examined by comparing a full model in which parameter estimates are allowed to differ in magnitude between males and females, with a reduced model in which parameter estimates are constrained to be equal across the sexes. In addition to those models a scalar model was tested. In a scalar model heritabilities are constrained to be equal across sexes, but total variances may be different. All nonstandardized variance components for females are constrained to be equal to a scalar multiple, k^2, of the male variance components, such that $h_f^2 = k^2 h_m^2$, $c_f^2 = k^2 c_m^2$, $e_f^2 = k^2 e_m^2$ and $d_f^2 = k^2 d_m^2$. As a result, the standardized variance components such as heritabilities are equal across sexes, even though the unstandardized components differ (Neale & Cardon, 1992). A path diagram of the applied twin model is shown in Figure 1.

Ethnic differences were examined in a similar fashion using a 10 group (ethnicity by sex by zygosity) univariate model in order to test for potential differences between AAs and EAs. A full model in which parameter estimates are allowed to differ in magnitude between EAs and AAs, was compared to a reduced model in which parameter estimates are constrained to be equal across ethnicities. In addition to those models a scalar model was tested in a similar fashion as done for sex models. All nonstandardized variance components

https://doi.org/10.1375/twin.8.5.492 Published online by Cambridge University Press

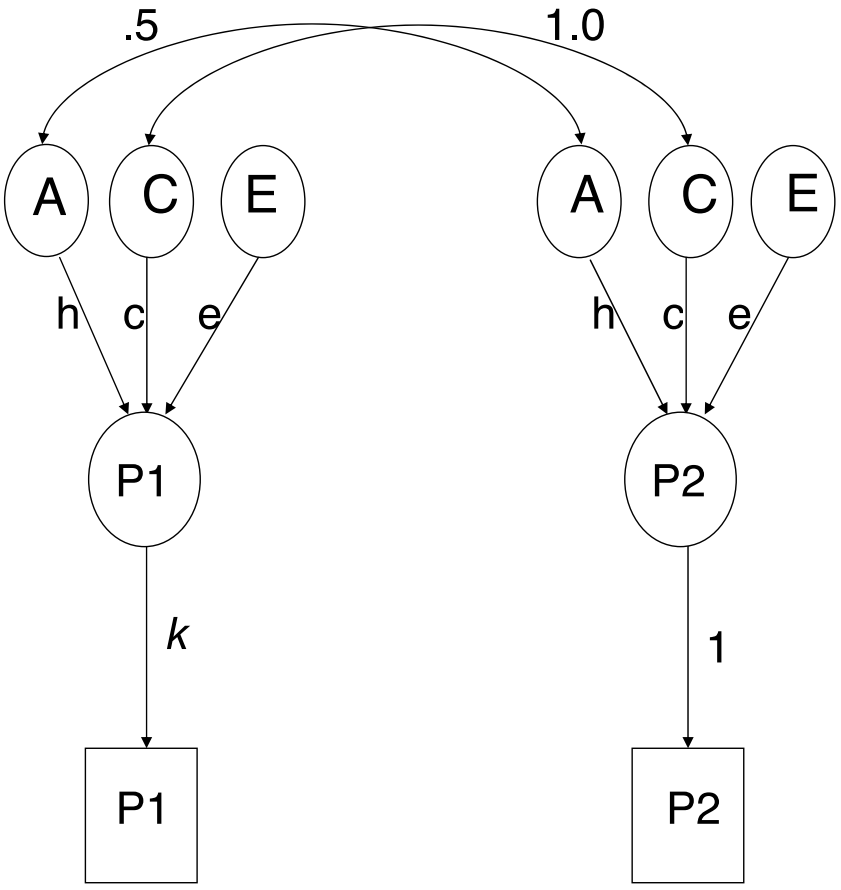

Figure 1

Path diagram for a univariate scalar model.

An opposite-sex twin pair is shown, twin 1 being female and twin 2 male. Observed phenotypes (P) for twin 1 and twin 2 are shown in squares; latent (i.e., unmeasured) factors are shown in circles. Correlations between additive genetic factors are 1 in MZ twins and .5 in DZ twins. Path coefficients (cf. regression coefficients) of observed variables on the different latent factors are shown in lower case: h = additive genetic effect, c = shared environmental effect, e = unique environmental effect, *k* = scalar factor. D, the dominance genetic influence, was also tested but is omitted to simplify the diagram.

for AAs are constrained to be equal to a scalar multiple, k^2, of the EA variance components. In these models heritabilities are equal across ethnic groups, even though the total variance differs.

Estimates of variance components and their confidence intervals were obtained by model fitting to the raw data by using normal theory maximum likelihood (Neale et al., 1999). This method allowed us to use the information provided by singleton twins, who contribute to the estimates of variance (but not covariance). The significance of A, C and D was tested by removing them sequentially in specific submodels. Together with testing for ethnic and sex differences this eventually leads to models that give the most parsimonious fit to the data, that is, models in which the pattern of variances and covariances is explained by as few parameters as possible. Submodels were compared with full models by hierarchic chi-square tests. The difference between minus twice the log-likelihood (–2lnL) for a submodel and that of the full model is approximately distributed as chi-square with degrees of freedom equal to the difference of the number of estimated parameters in the full model and the number of estimated parameters in the submodel.

Results

Sample characteristics are presented by ethnicity and sex in Table 1. Multiple regression analyses assessing ethnic and sex differences are also presented. EAs were significantly older (p = .03) and had a lower BMI (p = .03) than AAs. HDL was higher in females than males (p < .001) and in AAs than EAs (p < .001). For triglycerides a significant sex-by-ethnicity interaction (p = .02) was observed, with EA males exhibiting higher triglyceride levels than the other three ethnicity-by-sex categories. Results were similar with nonfasting participants excluded, except there was no ethnicity by sex interaction for triglycerides.

Separate model-fitting analyses in EA and AA twins allowed the investigation of sex differences and

https://doi.org/10.1375/twin.8.5.492 Published online by Cambridge University Press

Table 1

Descriptive Characteristics of a Sample of 212 European American and African American Males and Females

Characteristics	European American		African American		Tests for the effects of	
	Males	Females	Males	Females	Ethnicity	Sex
					p	*p*
n (subjects)[a]	54	52	54	52		
Age (y)	18.70 (3.73)	18.37 (2.64)	18.00 (3.11)	16.69 (2.87)	.03	*ns*
BMI (kg/m^2)	24.70 (4.77)	23.85 (5.90)	25.19 (5.76)	26.93 (6.96)	.03	*ns*
Total cholesterol (mmol/l)	4.23 (1.04)	4.09 (0.72)	4.02 (0.81)	4.17 (0.96)	*ns*	*ns*
High-density lipoprotein (mmol/l)	1.19 (0.32)	1.39 (0.30)	1.35 (0.26)	1.52 (0.47)	.001	.001
Low-density lipoprotein (mmol/l)	2.52 (0.76)	2.23 (0.57)	2.27 (0.74)	2.33 (0.85)	*ns*	*ns*
Triglycerides (mmol/l)	1.21 (0.56)	1.02 (0.53)	0.85 (0.31)	0.91 (0.35)	.001[b]	.01[c]

Note: Data are mean (*SD*) unless stated otherwise. *p* = probability value; *ns* = nonsignificant.

a = Maximum number of subjects is shown for each ethnicity by sex group, but total number for lipid variables varied slightly between 208 and 212.

b = Simple effect of ethnicity by sex interaction ($p = .02$) in males only.

c = Simple effect of ethnicity by sex interaction ($p = .02$) in European Americans only.

estimation of ethnic specific genetic and environmental variance components. The difference in log-likelihoods between the reduced (all parameters the same for males and females) and the full model (separate parameters for males and females) ranged from 1.30 (for HDL in EA) to 5.11 (for LDL in AA), and these chi-square values for three degrees of freedom were not significant. Hence, no sex differences were found for any of the lipid measurements within each ethnic group, so it was decided to collapse groups for sex in order to get reasonable sample sizes (20 or more pairs) for each zygosity group within ethnicity and more stable estimates for intraclass correlations. These correlations are shown in Table 2, after effects on lipid variables of fasting status, age, sex, ethnicity and the interactions between age, sex and ethnicity were regressed out. In general, intraclass correlations were higher in MZ than in DZ twins, indicating genetic influences. Intraclass correlations for AA MZ twins were slightly higher than those for EA MZ twins, except for triglycerides. For LDL, the MZ correlation in AA was higher than the MZ correlation in EA, while the DZ was smaller for AA than EA. This could indicate the importance of dominance effects in AA compared to EA. However, dominance effects were not significant in any of the models for any of the lipids. Adjustment for BMI or fasting status only had a minimal effect on the twin correlations (data not shown). BMI explained 4%, 5%, 8% and 6% of the total variance in total cholesterol, HDL, LDL and triglycerides, respectively, while fasting status explained 0.2%, 2%, 0% and 5% of the variance in the respective lipids.

Parameter estimates and 95% confidence intervals (CIs) of the best fitting models with EAs and AAs analyzed separately are presented in Table 3. Heritability estimates were slightly higher in AAs for all lipids except for triglyceride levels. For LDL in AAs a scalar model fitted best (difference between reduced and scalar model: $\chi^2 = 4.89$, $df = 1$, $p = .03$) indicating that the variance in females was higher than the variance in males. Estimates of the standardized genetic and environmental components of variance remained virtually unchanged after adjustment for BMI with a maximum difference of 1% (data not shown).

Finally, both ethnic groups were combined into one model to test for potential differences between EAs and AAs (Table 4). There was a significant ethnic difference in heritabilities for LDL (difference between reduced and full model: $\chi^2 = 10.91$, $df = 3$, $p = .01$). A lower estimate (69%) was observed for EAs than for AAs (92%). The chi-square values with 3 degrees of freedom comparing the reduced and the full models for other lipid components ranged from 0.6 (for HDL) to 5.1 (triglycerides), and were not significant. For triglycerides a scalar model fitted best (difference between reduced and scalar model: $\chi^2 = 5.05$, $df = 1$, $p = .02$). This implies the total variance for triglycerides in EA was higher compared to AA, but the heritabilities are the same (75%). Adjustment for BMI had a negligible effect on the standardized parameter estimates with a maximum difference of 1% (data not shown).

Table 2

Intraclass Correlations for MZ and DZ Pairs of European American and African American Twins

	European American		African American	
	MZ	DZ	MZ	DZ
N (pairs)	24	22	25	20
Total cholesterol	.66	.43	.87	.06
High-density lipoprotein	.66	.29	.72	.29
Low-density lipoprotein	.61	.41	.91	.14
Triglycerides	.63	.10	.74	–. 04

Note: Maximum number of complete pairs are shown although number of pairs is lower by one or two pairs for some analyses.

Lipid variables were adjusted for age, sex, ethnicity, and their interactions, and fasting status.

https://doi.org/10.1375/twin.8.5.492 Published online by Cambridge University Press

Table 3

Parameter Estimates and 95% Confidence Intervals of Best Fitting Models Fitted Separately for European American and African American Twins

	European American		African American	
	h^2 (95% CI)	e^2 (95% CI)	h^2 (95% CI)	e^2 (95% CI)
Total cholesterol	.75 (.52–.86)	.25 (.14–.48)	.89 (.76–.94)	.11 (.06–.23)
High-density lipoprotein	.75 (.44–.87)	.25 (.12–.56)	.77 (.56–.88)	.23 (.12–.44)
Low-density lipoprotein	.69 (.44–.83)	.31 (.17–.55)	.91 (.82–.95)[a]	.09 (.05–.18)[a]
Triglycerides	.75 (.40–.88)	.25 (.12–.60)	.74 (.52–.86)	.26 (.14–.48)

Note: Lipid variables were adjusted for age, sex, ethnicity, and their interactions, and fasting status.
CI = confidence interval.
a = for LDL there was a scalar effect with variance of females greater than variance of males.

Table 4

Parameter Estimates and 95% Confidence Intervals of Best Fitting Models from the Combined Analysis of European American and African American Twins

	European American		African American	
	h^2 (95% CI)	e^2 (95% CI)	h^2 (95% CI)	e^2 (95% CI)
Total cholesterol	.81 (.70–.88)	.19 (.12–.30)	—	—
High-density lipoprotein	.76 (.60–.85)	.24 (.15–.40)	—	—
Low-density lipoprotein	.69 (.45–.82)	.31 (.18–.55)	.92 (.83–.95)	.08 (.04–.17)
Triglycerides[a]	.75 (.50–.84)	.25 (.15–.41)	—	—

Note: — indicates that parameter estimates for European American and African American twins could be set equal in the best fitting model.
CI = confidence interval.
a = for triglycerides there was a scalar effect with variance of EAs greater than variance of AAs.
Lipid variables were adjusted for age, sex, ethnicity, and their interactions, fasting status, and body mass index.

The shared environmental components were consistently nonsignificant throughout all analyses for all lipids examined. Hence, they were omitted from all models.

Discussion

This study estimated the importance of genetic and environmental factors on variation in total cholesterol, HDL, LDL and triglycerides, in a sample of young AA and EA twins from the south-eastern United States. In this first twin study to include AAs, no ethnic differences were found in heritability estimates except for LDL, where AAs exhibited higher estimates compared to EAs.

Our findings largely confirm the somewhat paradoxical finding of a healthier lipid profile in AAs starting in childhood (Gillum, 1999; Srinivasan et al., 1991), in spite of the poorer health behaviors and higher prevalence of other risk factors shown in AA teenagers than in their EA peers (Gans et al., 2003; Gordon-Larsen et al., 1999; Kimm et al., 2001; Li et al., 2003; Weiss et al., 2005). It has been pointed out that these differences could not be accounted for by environmental factors and hence are more likely to be of genetic origin (Sprafka et al., 1992). There were significant ethnic differences in the mean levels, with higher HDL in AAs and higher triglyceride levels in EA males than in the other three ethnicity-by-sex categories. One explanation for the ethnic differences in HDL levels is the lower hepatic lipase activity in AAs than EAs (Wilson, 2000). A –514C→T polymorphism in the hepatic lipase gene (LIPC) has been found to be three times as common in AAs than in EAs (Vega et al., 1998) and has been associated with lower hepatic lipase activity and higher HDL concentrations. The LDLR T1733C locus may explain ethnic differences in triglyceride levels (Davis et al., in press).

It is worth noting that our study is the first twin study to estimate the heritability of lipids in AAs, and the proportion of variance in lipid levels explained by genetic factors was estimated to be very similar in AA and EA twins. The lack of sex differences in heritability estimates observed in this study is in accordance with results in previous studies in Caucasian twins, as reviewed by Snieder et al. (1999). A separate analysis of AA and EA showed that heritability estimates were slightly higher in AAs than in EAs. The intraclass correlations for LDL were suggestive of a dominance effect in AAs. However, dominance was not significant for any of the lipids and larger studies in AA twins would be needed to confirm the importance of dominance in LDL. Interestingly, scalar effects were present with the total variance of LDL in female AAs higher than that in male AAs, and where the total variance of triglycerides in EAs was larger compared to the variance in AAs; these, however, do not imply differences in the relative influence of genetic and environmental effects. Difference in variance could indicate individual

https://doi.org/10.1375/twin.8.5.492 Published online by Cambridge University Press

differences (i.e., in lifestyle) between groups, or could be an effect of randomness due to the small sample size. All heritabilities exceeded 50%, indicating the importance of genetic effects in the variation of lipids, and adjustment for BMI had virtually no effect on these heritability estimates. There was a significant ethnic difference in genetic and environmental variance component estimates for LDL. However, 3 years of intensive lifestyle intervention (diet and exercise) on a large multiethnic prediabetic cohort did not result in any changes in LDL levels (Dagogo-Jack, 2005; Ratner et al., 2005). Thus, the practical implications of greater heritability of LDL in AAs may be few.

While AAs and EAs share some common ancestry, ethnic variations in genetic factors appear to be important determinants of cardiovascular risk. A recent commentary (Risch et al., 2002) strongly advocated self-identification of ethnic group, as used here, for purposes of human categorization in biomedical and genetic research. The classic twin study is established as the ideal study design to estimate the relative contribution of genetic and environmental factors to the variance of traits and diseases in human populations (Snieder & MacGregor, 2003), but without actual measurement of specific genes or environments, it cannot attribute the ethnic difference in mean values to either of these factors. This study does show that the observed difference in mean values did not correspond to many differences in genetic and environmental variability between ethnic groups. However, the fact that a similar amount of variation is explained by genetic factors within different ethnic groups does not exclude the possibility that the actual genes responsible for these effects may differ or that the same genes may have different impact between ethnic groups. For example, polymorphisms influencing HDL and triglyceride levels such as the LIPC –514C→T (Vega et al., 1998) or the LDLR T1733C locus (Davis et al., in press) may have different effects in AA and EA populations because they show considerable ethnic differences in allele frequencies.

One limitation of the present study is the relatively small sample size of our twin study, which means power to detect ethnic or sex difference in the heritability of lipids was limited. Further twin studies with large sample sizes involving multiple ethnic groups are warranted. A second limitation is the inclusion of nonfasting participants. However, inspection of fasting twin correlations suggests that it did not affect our results substantially. Postprandial status may affect triglyceride but not HDL or total cholesterol measurements (Craig et al., 2000).

In conclusion, we confirm a healthier lipid profile in AA youth. Although limited by modest sample size and power, we find no major differences in heritability estimates for AAs and EAs, with heritability estimates in AAs consistent with previous research in Caucasian twins. The factors responsible for the ethnic differences in mean HDL and triglyceride levels need to be explored in future studies.

Acknowledgment

This study was supported by NIH Grant HL56622 and a State of Georgia Biomedical Initiative grant to the Georgia Center for the Prevention of Obesity and Related Disorders. Special thanks go to the study participants and staff.

References

Beekman, M., Heijmans, B. T., Martin, N. G., Pedersen, N. L., Whitfield, J. B., DeFaire, U., van Baal, G. C., Snieder, H., Vogler, G. P., Slagboom, P. E., & Boomsma, D. I. (2002). Heritabilities of apolipoprotein and lipid levels in three countries. *Twin Research, 5*, 87–97.

Berenson, G. S., Wattigney, W. A., Tracy, R. E., Newman, W. P., 3rd, Srinivasan, S. R., Webber, L. S., Dalferes, E. R., Jr., & Strong, J. P. (1992). Atherosclerosis of the aorta and coronary arteries and cardiovascular risk factors in persons aged 6 to 30 years and studied at necropsy (The Bogalusa Heart Study). *American Journal of Cardiology, 70*, 851–858.

Cholestech Corporation. (2001). *Technical brief: The accuracy and reproducibility of a rapid, fingerstick method for measuring a complete lipid profile is comparable to a reference laboratory method.* Hayward, CA: Cholestech.

Clark, L. T., Ferdinand, K. C., Flack, J. M., Gavin, J. R., 3rd, Hall, W. D., Kumanyika, S. K., Reed, J. W., Saunders, E., Valantine, H. A., Watson, K., Wenger, N. K., & Wright, J. T. (2001). Coronary heart disease in African Americans. *Heart Disease, 3*, 97–108.

Craig, S., Amin, R., Russell, D., & Paradise, N. (2000). Blood cholesterol screening: Influence of fasting state on cholesterol results and management decisions. *Journal of General Internal Medicine, 15*, 395–399.

Dagogo-Jack, S. (2005). Primary prevention of cardiovascular disease in pre-diabetes: The glass is half full and half empty. *Diabetes Care, 28*, 971–972.

Davis, C. L., Wang, X., Treiber, F. A., & Snieder, H. (in press). Genetic and environmental determinants of lipid profile in black and white youth: A study of four candidate genes. *Ethnicity & Disease*.

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. (2001). Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *Journal of the American Medical Association, 285*, 2486–2497.

Friedewald, W. T., Levy, R. I., & Fredrickson, D. S. (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical Chemistry, 18*, 499–502.

https://doi.org/10.1375/twin.8.5.492 Published online by Cambridge University Press

Gans, K. M., Burkholder, G. J., Risica, P. M., & Lasater, T. M. (2003). Baseline fat-related dietary behaviors of white, hispanic, and black participants in a cholesterol screening and education project in New England. *Journal of the American Dietetic Association, 103*, 699–706.

Gillum, R. F. (1999). Distribution of waist-to-hip ratio, other indices of body fat distribution and obesity and associations with HDL cholesterol in children and young adults aged 4–19 years: The Third National Health And Nutrition Examination Survey. *International Journal of Obesity and Related Metabolic Disorders, 23*, 556–563.

Gordon-Larsen, P., McMurray, R. G., & Popkin, B. M. (1999). Adolescent physical activity and inactivity vary by ethnicity: The National Longitudinal Study Of Adolescent Health. *Journal of Pediatrics, 135*, 301–306.

Iliadou, A., Lichtenstein, P., de Faire, U., & Pedersen, N. L. (2001). Variation in genetic and environmental influences in serum lipid and apolipoprotein levels across the lifespan in Swedish male and female twins. *American Journal of Medical Genetics, 102*, 48–58.

Iselius, L. (1979). Analysis of family resemblance for lipids and lipoproteins. *Clinical Genetics, 15*, 300–306.

Jackson, R. W., Snieder, H., Davis, H., & Treiber, F. A. (2001). Determination of twin zygosity: A comparison of DNA with various questionnaire indices. *Twin Research, 4*, 12–18.

Kimm, S. Y., Barton, B. A., Obarzanek, E., McMahon, R. P., Sabry, Z. I., Waclawiw, M. A., Schreiber, G. B., Morrison, J. A., Similo, S., & Daniels, S. R. (2001). Racial divergence in adiposity during adolescence: The NHLBI Growth And Health Study. *Pediatrics, 107*, E34.

Li, S., Chen, W., Srinivasan, S. R., Bond, M. G., Tang, R., Urbina, E. M., & Berenson, G. S. (2003). Childhood cardiovascular risk factors and carotid vascular changes in adulthood: The Bogalusa Heart Study. *Journal of the American Medical Association, 290*, 2271–2276.

Neale, M. C., Boker, S. M., Xie, G., & Maes, H. H. (1999). *Mx: Statistical modeling*. Richmond, VA: Department of Psychiatry, Virginia Commonwealth University.

Neale, M. C., & Cardon, L. R. (1992). *Methodologies for genetic studies of twins and families*. Dordrecht, the Netherlands: Kluwer Academic.

Ratner, R., Goldberg, R., Haffner, S., Marcovina, S., Orchard, T., Fowler, S., Temprosa, M., Diabetes Prevention Program Research Group. (2005). Impact of intensive lifestyle and metformin therapy on cardiovascular disease risk factors in the Diabetes Prevention Program. *Diabetes Care, 28*, 888–894.

Risch, N., Burchard, E., Ziv, E., & Tang, H. (2002). Categorization of humans in biomedical research: Genes, race and disease. *Genome Biology, 3*, comment 2007.1–2007.12.

Snieder, H., Boomsma, D. I., & van Doornen, L. J. P. (1999). Dissecting the genetic architecture of lipids, lipoproteins and apolipoproteins. Lessons from twin studies. *Arteriosclerosis, Thrombosis and Vascular Biology, 19*, 2826–2834.

Snieder, H., & MacGregor, A. J. (2003). Twin methodology. In D. N. Cooper (Ed.), *Encyclopedia of the human genome*. London: Nature Publishing Group.

Snieder, H., & Treiber, F. A. (2002). The Georgia cardiovascular twin study. *Twin Research, 5*, 497–498.

Snieder, H., van Doornen, L. J., & Boomsma, D. I. (1997). The age dependency of gene expression for plasma lipids, lipoproteins, and apolipoproteins. *American Journal of Human Genetics, 60*, 638–650.

Sprafka, J. M., Norsted, S. W., Folsom, A. R., Burke, G. L., & Luepker, R. V. (1992). Life-style factors do not explain racial differences in high-density lipoprotein cholesterol: The Minnesota heart survey. *Epidemiology, 3*, 156–163.

Srinivasan, S. R., Wattigney, W., Webber, L. S., & Berenson, G. S. (1991). Race and gender differences in serum lipoproteins of children, adolescents, and young adults-emergence of an adverse lipoprotein pattern in white males: The Bogalusa heart study. *Preventive Medicine, 20*, 671–684.

Vega, G. L., Clark, L. T., Tang, A., Marcovina, S., Grundy, S. M., & Cohen, J. C. (1998). Hepatic lipase activity is lower in African American men than in white American men: Effects of 5' flanking polymorphism in the hepatic lipase gene (LIPC). *Journal of Lipid Research, 39*, 228–232.

Weiss, R., Taksali, S. E., Tamborlane, W. V., Burgert, T. S., Savoye, M., & Caprio, S. (2005). Predictors of changes in glucose tolerance status in obese youth. *Diabetes Care, 28*, 902–909.

Whitty, C. J., Brunner, E. J., Shipley, M. J., Hemingway, H., & Marmot, M. G. (1999). Differences in biological risk factors for cardiovascular disease between three ethnic groups in the Whitehall II study. *Atherosclerosis, 142*, 279–286.

Wilson, P. W. (2000). Lipids, lipases, and obesity: Does race matter? *Arteriosclerosis, Thrombosis and Vascular Biology, 20*, 1854–1856.

https://doi.org/10.1375/twin.8.5.492 Published online by Cambridge University Press