The association of candidate gene variants with blood lipids in the NHANES III study

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Background

Numerous studies have shown a strong relationship between cardiovascular disease and high levels of serum total cholesterol (STC), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and an inverse relationship between high-density lipoprotein cholesterol (HDL-C). In the present study, we examined the association between postulated candidate genes and serum lipid levels and its interactions with environment factors in the Third National Health and Nutrition Examination Survey (NHANES III), a weighted nationally-representative sample of the U.S. population.

Methods

We used DNA data available from 7,159 participants aged 12 and older examined during the second phase of NHANES III (1991-1994). Associations between the 24 genetic variants in 15 candidate genes and the cardiovascular disease risk factors, HDL, LDL, STC, and TG, were examined, either in three-level genetic models or in a dominant mode of inheritance in linear regression models, controlling for demographic and environmental factors, including age, sex, education level, body mass index, alcohol intake, dietary fat intake, physical activity, and smoking status. To limit the effect of possible interactions between race/ethnicity and the genetic variants, all models were stratified by self-reported race/ethnicity (i.e., non-Hispanic white, non-Hispanic black, and Mexican American).

Results

Two SNPs in APOE (rs7412 and rs429358) were found to be significantly associated with LDL-C and STC levels in all three ethnic groups after adjusting for the study risk factors. The APOE rs7412 variant was associated with HDL-C levels in non-Hispanic blacks, and APOE rs429358 variant was associated with TG in non-Hispanic whites and Mexican Americans. Variants within ADH1C, F2, MTHFR, MTRR, PON1, SERPINE1, and TNF were also found to be individually associated with at least one of the measures of blood lipids for least one of the race/ethnicity subgroups.

Conclusion

The results of our study support previously reported evidence of genes associated with serum HDL-C, LDL-C STC, and TG levels. The clarification of the genetic contribution and further examination of gene-gene and gene-environment interactions may aid in the identification of individuals with an increased susceptibility to cardiovascular disease and the promotion of the future interventions.