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GENOME-WIDE LINKAGE ANALYSIS OF CAROTID ARTERY LUMEN DIAMETER IN AMERICAN INDIANS: THE STRONG HEART FAMILY STUDY

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Background: Population-based studies have shown a correlation between carotid artery lumen diameter and risk of aortic aneurysm formation. Chromosomal regions associated with inter-individual variation in carotid artery lumen diameter are unknown.

Methods: Carotid ultrasonography and genotyping were performed in American Indian participants in the Strong Heart Family Study (SHFS) to identify chromosomal regions harboring novel genes associated with inter-individual variation in carotid artery lumen diameter. Genome-wide linkage analysis used standard variance component linkage methods, implemented in SOLAR, based on multipoint identity-by-descent matrices estimated by Markov Chain Monte Carlo methods with the program Loki.

Results: Carotid artery measurements were available in 1164 Arizona participants, 1141 North and South Dakota participants and 1133 Oklahoma participants. Genome-wide linkage analysis revealed a significant evidence for linkage for a locus for left carotid artery diastolic and systolic lumen diameter in Arizona SHFS participants on chromosome 7 at 120 cM (lod=4.85 and 3.77, respectively, after sex and age adjustment, and lod=3.33 and 3.00, respectively, after adjustment for sex, age, height, weight, systolic and diastolic blood pressure and current smoking). Other regions with suggestive evidence of linkage for left carotid artery diastolic and systolic lumen diameter was found on chromosome 12 at 153 cM (lod=2.20 and 2.60, respectively, after sex and age adjustment, and lod=2.48 and 2.18, respectively, after full covariate adjustment) in Oklahoma SHFS participants; suggestive linkage for right carotid artery diastolic and systolic lumen diameter was found on chromosome 9 at 154 cM (lod=2.72 and 3.19, respectively after sex and age adjustment, and lod=2.34 and 2.29, respectively, after full covariate adjustment) in Oklahoma SHFS participants.

Conclusion: We found significant evidence for loci influencing carotid artery lumen diameter on chromosome 7q and suggestive linkage on chromosomes 12q and 9q. Further studies are needed to determine the genes and variants contained in these regions that are responsible for the observed linkage results.