# Genetic Link between Alzheimer's Disease, Lipid Metabolism, and Coronary Artery Disease Revealed

A group of researchers systematically evaluated the genetic overlap between Alzheimer's disease (AD) (a neurodegenerative disorder causing memory loss and cognitive decline), lipid profiles, and coronary artery disease (CAD) traits using large-scale genetic data and robust analytical methods.

## Study

The relationship between AD and various lipid traits, representing eight major lipid classes, was thoroughly examined.

These lipid classes included fatty acyls, glycerophospholipids, high-density lipoproteins (HDL) and low-density lipoproteins (LDL), neutral lipids (triglycerides), medium-chain fatty acids, steroids (total cholesterol), and sphingolipids.

The study utilized Genome-Wide Association Study (GWAS) summary data from large-scale research consortia, including Cooperative Health Research in the Region of Augsburg (KORA), Twins United Kingdom (TwinsUK), and the Global Lipids Genetics Consortium, among others.

The analysis also considered the relationship between AD and seven CAD traits, using data sourced from the Lee Lab for Statistical Genetics and the CARDIoGRAMplusC4D consortium.

To explore the genetic relationships, the study employed linkage disequilibrium score regression (LDSC) and local analysis of [co]variant association (LAVA) methods at both Single Nucleotide Polymorphism (SNP) and gene levels.

Additionally, the study conducted gene-based association analyses to identify overlapping genes between AD, lipids, and CAD traits, employing multi-marker analysis of genomic annotation (MAGMA) within the Functional Mapping and Annotation (FUMA) platform.

The research identified significant global genetic correlations between AD and specific lipid traits such as LDL, triglycerides, and total cholesterol and a positive correlation between AD and various CAD traits.

However, Mendelian randomization analyses did not support a causal link, suggesting shared genetic susceptibility as a more plausible explanation. Local genetic correlation analyses pinpointed specific genomic loci contributing to these associations, offering further insight into the complex genetic landscape linking AD with cardiovascular health.

## Findings

Initially, the researchers utilized LDSC to assess and quantify SNP-level global genetic correlations across 13 lipid traits, seven CAD traits, and AD.

This analysis revealed significant global genetic correlations between AD and specific lipid traits, particularly triglycerides, LDL, and total cholesterol.

Similarly, strong correlations were found between AD and several CAD traits, including angina pectoris (chest pain due to reduced blood flow to the heart), cardiac dysrhythmias (abnormal heart rhythms), and coronary arteriosclerosis (hardening and narrowing of heart arteries). These results suggested that shared genetic components might predispose individuals to both AD and certain lipid and CAD traits.

The study applied bi-directional two-sample Mendelian randomization (2SMR) analyses to test for potential causal associations between these traits. However, the 2SMR analyses did not provide evidence for a causal relationship between AD, lipids, and CAD traits, indicating that the observed correlations might be due to shared genetic susceptibility rather than direct causal links.

The researchers conducted gene-based analyses to delve deeper into the genetic overlap, identifying genome-wide significant (GWS) genes shared by AD, lipids, and CAD traits. Notably, genes such as Apolipoprotein E (APOE), APOC1, and Translocase of Outer Mitochondrial Membrane 40 (TOMM40) overlap AD and several CAD traits, reinforcing the genetic connection between these disorders.

Additionally, Fisher's combined p-value (FCP) method was employed to identify shared genes that reached GWS across AD, lipids, and CAD traits, highlighting genes that might play a critical role in the pathogenesis of these conditions.

Furthermore, local genetic correlation analysis using the LAVA method was conducted to identify specific genomic regions contributing to the genetic correlations observed at the global level. This analysis pinpointed several loci, particularly on chromosomes 6, 8, 17, and 19, significantly associated with AD and various lipid and CAD traits.

Among these, the locus on chromosome 19 was notably implicated across multiple traits, suggesting a hotspot for shared genetic influences.

Finally, the study compared the results obtained from LDSC and LAVA to assess the consistency of the findings. While both methods identified significant genetic correlations, some discrepancies were observed, particularly in the direction of effects, emphasizing the importance of using multiple analytical approaches to understand genetic relationships comprehensively.

## Conclusion

This study systematically assessed genetic correlations between AD, 13 lipid traits, and seven CAD traits using advanced statistical tools. Significant correlations were found between AD and specific lipids (LDL, triglycerides, total cholesterol) and all CAD traits, indicating shared genetic susceptibility.

However, Mendelian randomization analyses found no causal relationships, suggesting these associations may stem from shared genetics rather than direct causality. Local genetic analysis identified key loci on chromosomes 6, 8, 17, and 19 contributing to these associations.

**Source:**

https://www.news-medical.net/news/20240820/Study-reveals-genetic-link-between-Alzheimers-disease-lipid-metabolism-and-coronary-artery-disease.aspx