Researchers confirm genetic link between Alzheimer's and heart disease

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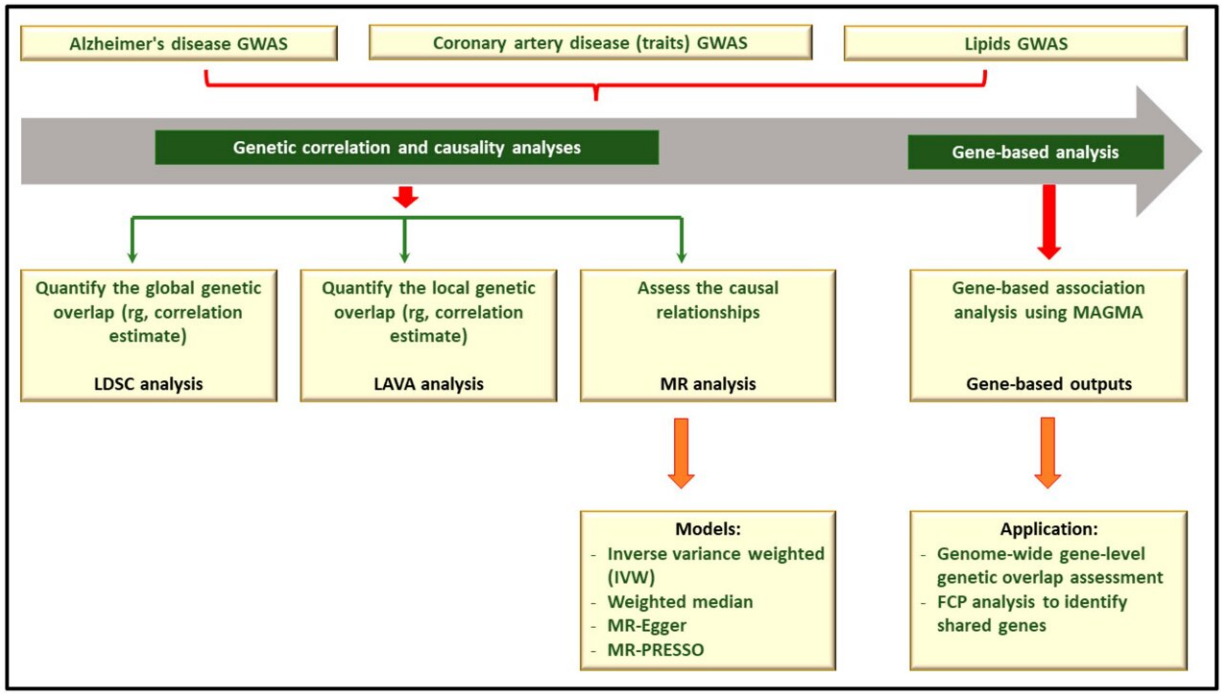

Study design and workflow: assessing shared genetic associations between AD, lipids, and CAD traits. FCP: Fisher's combined p value; MAGMA–multi-marker analysis of genomic annotation; GWAS: genome-wide association studies; LDSC: linkage disequilibrium score regression; LAVA: local analysis of [co]variant association; MR: Mendelian randomization; MR-PRESSO: Mendelian randomization pleiotropy residual sum and outlier.

Researchers at Edith Cowan University's (ECU's) Centre for Precision

Health have uncovered a significant genetic connection between Alzheimer's disease (AD) and several coronary artery disease (CAD) related disorders and lipid classes, offering opportunities to improve health outcomes across two of the more common causes of death in Australia.

"Investigating genetic overlap between Alzheimer's disease, lipids and coronary artery disease" has been published in the *International Journal of Molecular Science.*

The new research has found that several heart disease-related factors like angina, arteriosclerosis, ischemic heart disease, myocardial infarction, and coronary artery disease as well as lipids like cholesterol, triglycerides and both high- and low-density lipoproteins (HDL and LDL) could share similar biological origins with AD.

This means that some of the same genes played a role in or are associated across these conditions.

"There is considerable evidence from observational and other studies to support a connection between these conditions, however the intricate biological mechanisms of AD are poorly understood, and its relationship with lipids and CAD traits remains unresolved," lead researcher and Centre for Precision Health Ph.D. candidate Artika Kirby said.

"Our study employed a genetic approach to investigate the intricate relationships of these comorbid conditions, providing new insights into their shared biological underpinnings of these conditions. I am optimistic that our findings open new avenues of research that have the potential to enhance the lives of millions, worldwide."

"The Centre for Precision Health's use of advanced statistical genetics approaches is significantly contributing to our understanding of the

relationships across many of today's major health conditions—this study emphasizes the strength of this approach," Professor Simon Laws, Director of the Centre for Precision Health and co-supervisor of the study, remarked.

Dementia, of which AD is the major cause, and coronary artery or heart disease, are the two leading underlying causes of death in Australians. Researchers say there may be more to link these conditions than just their association with poor health outcomes.

Evidence increasingly links CAD with cognitive impairment and the risk of dementia with research suggesting that individuals with CAD experience an accelerated cognitive decline following diagnosis and CAD patients have a 26% higher relative risk of dementia. However, the nature of the relationship and the underpinning mechanisms for CAD's association with AD and cognitive impairment remains unclear.

The connection between CAD and AD may partly reflect shared risk factors such as dyslipidemia and inflammation. Lipid disorders and CAD considerably impact human health and are recognized as a substantial risk factor for AD, just as a relationship between CAD and AD has been reported.

There is also the potential for shared genetic predispositions across all of these factors.

"By applying genetic approaches to gain a deeper understanding of the relationship between AD and Coronary Heart disease—the two leading causes of death in Australia—we have uncovered novel insights into the underlying mechanisms linking these conditions," NHMRC Emerging Leadership Fellow and project co-supervisor Dr. Emmanuel Adewuyi added.

"These insights could translate into improvements in patient care and outcomes for these two leading health issues—not only in Australia but around the world."

More information: Artika Kirby et al, Investigating Genetic Overlap between Alzheimer's Disease, Lipids, and Coronary Artery Disease: A Large-Scale Genome-Wide Cross Trait Analysis, *International Journal of Molecular Sciences* (2024). DOI: 10.3390/ijms25168814

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