Researchers identify variation in gene PLD3 can increase risk of late-onset Alzheimer's disease

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(Medical Xpress)—A new study, part-funded by the Medical Research Council (MRC), the Wellcome Trust and Alzheimer's Research UK, has shown that a fault in a gene called phospholipase D3 (PLD3) can contribute to the overproduction of amyloid-beta in the brain. Increased levels of this chemical are associated with an increased chance of developing Alzheimer's disease and the results show that, in certain cases, this can double an individual's risk.

An international team of researchers in the UK and the US have been using genome-wide association studies (GWAS) to identify common genetic traits in the population that can influence a person's risk of contracting Alzheimer's disease after the age of 60 (known as Late Onset Alzheimer's Disease or LOAD). They then cross-analysed the data from the GWAS studies using a process known as whole-exome sequencing on 14 families with four or more members affected by Alzheimer's. Focussing on families heavily affected by the disease, the team used a new process to identify less common genes that could have the most severe effect.

By improving researchers' understanding of how this gene's activity is linked to amyloid-beta production and Alzheimer's disease, this study will open up new avenues of research for drug development and could potentially help identify people who are more vulnerable to the disease.
Dr Carlos Cruchaga the study's lead author at Washington University School of Medicine in St. Louis said "We were very excited to be able to identify a gene that contains some of these rare variants. And we were surprised to find that the effect of the gene was so large. After adjusting for other factors that can influence risk for the disease, we found that people with certain gene variants were twice as likely as those who didn't have the variants to develop Alzheimer's."

Professor John Hardy who led the UK work at University College London (UCL) and was funded by the Medical Research Council and the Wellcome Trust said, "The use of the new technologies of whole genome and whole-exome sequencing in Alzheimer's disease is now yielding a rich harvest of genetic variants which influence our risks of developing disease. These re-enforce the critical role of amyloid deposition and breakdown in the brain as one of the 'main events' that can cause Alzheimer's disease."

Rebecca Wood, Chief Executive of Alzheimer's Research UK, the UK's leading dementia research charity, said, "Advances in genetic technology are allowing researchers to understand more than ever about the genetic risk factors for the most common form of Alzheimer's. This announcement, made just off the back of the G8 dementia research summit, is a timely reminder of the progress that can be made by worldwide collaboration. We know that late-onset Alzheimer's is caused by a complex mix of risk factors, including both genetic and lifestyle. Understanding all of these risk factors and how they work together to affect someone's likelihood of developing Alzheimer's is incredibly important for developing interventions to slow the onset of the disease. Alzheimer's Research UK is proud to have contributed to this discovery, both by funding researchers and through the establishment of a DNA collection that has been used in many of the recent genetic discoveries in Alzheimer's."

Provided by Medical Research Council


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