Differences in blood biomarkers in people with genetic risk of Alzheimer's

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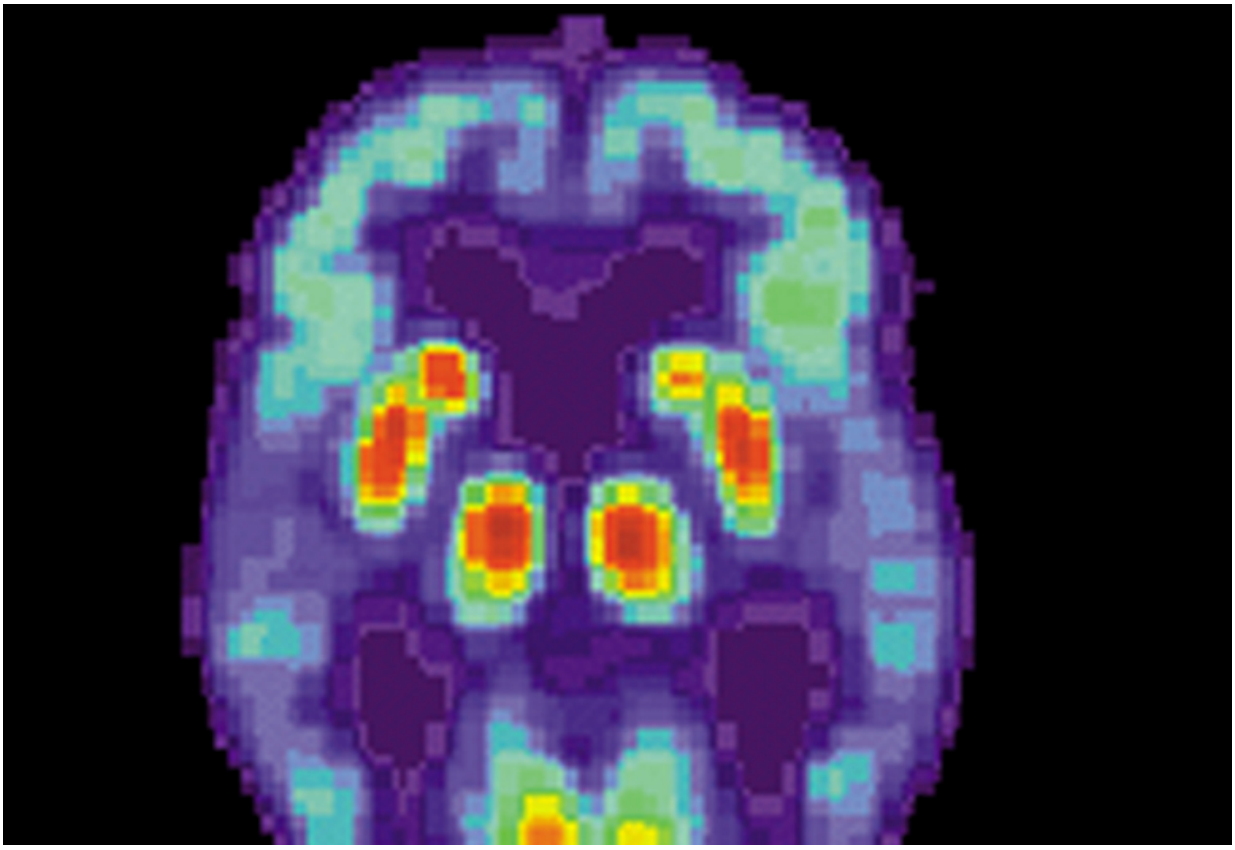

PET scan of a human brain with Alzheimer's disease. Credit: public domain

Researchers at the University of Glasgow have conducted the largest study to date on a wide range of common blood biomarkers and show clear differences in people at genetic risk of Alzheimer's disease.

The research—published today in the *Journal of Alzheimer's Disease* and using data from nearly 400,000 people in the UK Biobank—found relatively-large associations of neuro-inflammatory and cholesterol biomarkers, such as low-density lipoprotein levels, in people with a genetically-high risk of Alzheimer's disease.

Alzheimer's disease is the most common form of dementia, and is believed to be the result of interactions between genetic and environmental risk factors.

The Alzheimer's disease (AD) susceptibility gene—Apolipoprotein e4 (APOE e4)—is a major genetic risk factor for the disease, with one copy of the gene found in around 25% of the population, increasing risk of dementia by at least three times. Two copies of the gene are found in around 2% of the population, increasing risk of dementia by around 15 times. APOE e4 is the largest common single genetic risk factor for AD and cognitive decline behind increasing age.

The study aimed to investigate the potential influence of APOE e4 on common blood biomarkers, whilst also taking into account lifestyle factors, in both people with confirmed AD and those at a genetically-high risk for the disease.

The researchers looked at a wide range of blood biomarkers—such as cholesterols, markers of inflammation, vitamin D and IGF-1 levels, sex-specific hormones and renal function—in people carrying the APOE e4 genotype (compared with the "neutral" e3 carriers) to better understand the mechanisms of AD and dementia risk.

The research also found that a previously suggested risk factor of a low IGF-1 level, based on studies including people diagnosed with AD, might in fact be the opposite, with a raised IGF-1 level a potential risk factor. Previous studies also reported an association between APOE e4

and higher vitamin D levels; however, this study found decreased levels vitamin D, suggesting higher levels could be protective for people at risk for AD.

Dr. Donald Lyall, lecturer in Public Health at the University's Institute of Health and Wellbeing and senior author on the study, said: "Our research confirmed that the APOE e4 genotype predicted subsequent dementia. But, more importantly, by looking at such a large sample size and such a wide range of biomarkers—both in patients with the disease and those currently non-demented but at high genetic risk– we were able to get a 'big picture' look at the role of common biomarkers and this gene, which is considered to be dementia-causing. Our findings of relatively-large associations between e4 genotype with neuro-inflammatory biomarkers and elevated cholesterol levels, reinforces that these biological pathways are important to our understanding of common, late-onset Alzheimer's disease. While these findings could suggest biomarkers for dementia, further studies are needed to fully determine their role in dementia, both in those with a high genetic risk for Alzheimer's disease and more generally."

Lead author Dr. Amy Ferguson added: "We hope that, by continuing to understand biomarkers of those at genetic risk of AD, we can one day use them in early detection of AD and, hopefully, potential pathways for future prevention, management and treatment options."

The study looked at data from 395,769 participants of White European ancestry.

The paper, "Alzheimer's disease Susceptibility Gene Apolipoprotein E (APOE) and Blood Biomarkers in UK Biobank (N = 395,769)," is published in *Journal of Alzheimer's disease*.

More information: Amy C. Ferguson et al. Alzheimer's Disease

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Susceptibility Gene Apolipoprotein E (APOE) and Blood Biomarkers in UK Biobank (N = 395,769), *Journal of Alzheimer's Disease* (2020). DOI: 10.3233/JAD-200338

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