Certain genetic variant in Alzheimer's disease linked to African ancestry

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For individuals of African ancestry, the *APOE* ε3 R145C missense

variant is associated with an increased risk for Alzheimer disease (AD), according to a study published in the Feb. 21 issue of the *Journal of the American Medical Association*.

Yann Le Guen, Ph.D., from Stanford University in California, and colleagues examined whether amino acid changes to *APOE* specific to individuals of African ancestry modulate the risk for AD. The study combined a case-control study using a sequenced discovery sample (stage 1; 2,888 cases and 4,957 controls) followed by two microarray imputed datasets (stage 2, internal replication [1,201 cases and 2,744 controls] and stage 3, external validation [733 cases and 19,406 controls]). Two *APOE* missense variants were assessed (R145C and R150H). Individuals included in the study were of African ancestry.

The researchers found that R145C was present in 4.8 and 1.5 percent of participants with AD and controls in stage 1 and was associated with an increased risk for AD (odds ratio, 3.01; 95 percent confidence interval, 1.87 to 4.85) and reported younger age at AD onset (β, −5.87 years). In stage 2, the association with increased AD risk was replicated; R145C was present in 4.7 and 2.7 percent of those with AD and controls (odds ratio, 2.20; 95 percent confidence interval, 1.04 to 4.65), with concordant results observed in stage 3 (R145C present in 3.8 and 2.7 percent, respectively; odds ratio, 1.90; 95 percent confidence interval, 0.99 to 3.64). In stages 2 and 3, the association with earlier AD onset was also replicated (β, −5.23 and −10.15 years, respectively).

"With additional external validation, the findings may inform AD genetic risk assessment in individuals of African ancestry," the authors write.

More information: Yann Le Guen et al, Association of African Ancestry–Specific APOE Missense Variant R145C With Risk of Alzheimer Disease, *JAMA* (2023). DOI: 10.1001/jama.2023.0268