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A Common DIO2 Polymorphism And Alzheimer's Disease Dementia in African And European Americans.

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Abstract

CONTEXT: A common single nucleotide polymorphism in DIO2, Thr92AlaD2, has been associated with a transcriptome typically found in neurodegenerative diseases in postmortem human brain tissue.

OBJECTIVE: To determine whether Thr92AlaD2 is associated with incident Alzheimer's disease (AD).

DESIGN: Population-based study; human brain tissue microarray.

SETTING: Community-based cohorts from Chicago, Illinois and northeastern Illinois, as well as religious clergymen from across the U.S. made up the primary population. A representative sample of the U.S. population was used for secondary analyses.

PARTICIPANTS: 3054 African (AA) and 9304 European Americans (EA).

MAIN OUTCOME MEASURE: Incident AD.

RESULTS: In the primary population, AAs with Thr92AlaD2 had 1.3 times (95% CI, 1.02 to 1.68; P=0.048) higher odds of developing AD. AAs from a second population with Thr92AlaD2 had a trend towards increased odds of dementia (odds ratio (OR) 1.33; 95% CI, 0.99 to 1.78; P=0.06); they also exhibited 1.35 times higher odds of developing cognitive impairment not demented (CIND, 95% CI, 1.09 to 1.67; P=0.006). Meta-analysis showed that AAs with Thr92AlaD2 had 1.3 times increased odds of developing AD/dementia (95% CI, 1.07 to 1.58; P=0.008). In EAs there was no association between Thr92AlaD2 and AD, dementia, or CIND. Microarray of AA brain tissue identified transcriptional patterns linked to AD pathogenesis.

CONCLUSIONS: Thr92AlaD2 is associated with molecular markers known to underlie AD pathogenesis in AAs; this translates to an observed phenotype of increased odds of developing AD/dementia in AAs in these populations. Thr92AlaD2 may represent one factor contributing to racial discrepancies in incident AD.

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