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African Americans with thyroid gene variation more likely to develop Alzheimer's

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African Americans with a common genetic variation are at increased risk for developing Alzheimer's disease, while European Americans with the same variation are not, according to a study led by researchers at Rush University Medical Center. They published the study results in the February 22 online issue of the Journal of Clinical Endocrinology and Metabolism.

The genetic variation, known as Thr92AlaD2 polymorphism, affects a gene involved in the activation of thyroid hormone and occurs commonly; almost half the population are carriers of this polymorphism. The study found that African Americans with this polymorphism are 30 percent more likely to develop Alzheimer's disease dementia than the African American without the genetic polymorphism. Whereas in European Americans, this gene wasn't associated with increased risk of Alzheimer's. This is a remarkable juxtaposition.

"This correlation only shows up in African-Americans. We have some ideas but aren't sure why," said Elizabeth McAninch MD, study author and assistant professor of the Division of Endocrinology and Metabolism at Rush.

Discovery is twist in research that began with thyroid gland

The discovery was the latest twist in an investigation that began years ago in Rush's endocrinology division under the leadership of Dr. Antonio Bianco, a thyroid expert and the director of the present studies. Endocrinologists provide care for hormone imbalances that cause health problems.

The Thr92AlaD2 polymorphism affects an enzyme that activates thyroid hormones. The enzyme is most important when considering patients with a condition known as hypothyroidism, which occurs when there is insufficient thyroid hormone being produced by the thyroid gland. In most cases, this condition can be controlled with the standard treatment for hypothyroidism, a drug called levothyroxine. However, about 15 percent of patients treated with levothyroxine consistently say it doesn't help them feel better.

Wondering what was behind those reports, McAninch and colleagues at Rush previously obtained and analyzed brain tissue from the University of Miami Brain Bank from deceased Caucasian male organ donors who at their time of death were young and healthy, without known thyroid problems, to see if they could find any clues. To their surprise, the brains of the healthy donors who had the polymorphism displayed biomarkers that are known to play a role in neurodegenerative brain disease.

"This was a shock to us and deserved more investigation," McAninch recalled.

Researchers then drew on data from long-term studies of Alzheimer's

The endocrinologists then enlisted the help of Rush researchers who specialize in the issues of the aging brain, and the expanded team set to work with data from three long-term group studies done at Rush from 1993 to 2012 -; the Chicago Health and Aging Project (CHAP), the Religious Orders Study (ROS), and the Rush Memory and Aging Project (MAP).

The CHAP cohort includes 3656 participants, 2321 of whom are African American, who received cognitive testing in three-year cycles for more than 18 years. In ROS and MAP, 1,707 European American participants without known dementia were enrolled and had annual evaluations.

Again, McAninch and colleagues also continued to collaborate with the University of Miami Brain Bank to obtain and study brain tissue from young, healthy African American brain donors.

Through utilizing the CHAP data, which has both African American and European American participants, this unique racially-stratified outcome revealed itself. "That's when we saw this huge discrepancy in risk for Alzheimer's disease dementia," McAninch said.

Questions remain to be answered in future studies

Minorities tend to be understudied in medical research in general, and specifically there needs to be more, larger studies of African Americans to evaluate the risk of Alzheimer's, McAninch observed. "A strength of this study is credited to the amazing resource we have in these three cohort studies here at Rush, where we were able to look at the differences between African-

Americans and European-Americans," she says.

The Rush-led team is already planning the next inquiry, McAninch says, "to try to understand why African-Americans have this risk, while the European-Americans do not."

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