Race Modifies the Relationship between Alzheimer's Disease (AD) Biomarkers and Cognition in a Cohort of Middle-Aged Individuals with a Family History of AD

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Introduction

With the projected increase in Alzheimer's Disease (AD) over the coming decades, there is an increased urgency to find ways of preventing or delaying disease onset. The rate of AD for African American's (AAs) is 64% higher than for non-Hispanic White Americans (Whites)[1]. It is hypothesized that poor peripheral vascular function in combination with genetics, stress and inflammation may directly contribute to the accumulation of AD pathologic biomarkers Tau and amyloid[2,3]. These risk factors have been shown to more heavily affect AAs[4]. Additionally, the accumulation of AD biomarkers starts in middle age, years before onset of symptoms, making this an important target for intervention. We hypothesized that in a healthy middle-aged cohort at risk for AD by virtue of family history, (1) AD biomarkers in CSF differ by race, (2) worse cognition is related to higher burden of CSF biomarkers, and (3) the relationship between cognition and AD biomarkers differs by race.

Methods

The Association between Cardiovascular Risk and Preclinical Alzheimer's Disease Pathology (ASCEND) Study is a two-year observational study, which enrolled 82 cognitively normal, middle-aged (45 and older) adults including AAs and Whites at high risk for AD due to parental history. 30 AAs and 50 Whites were enrolled. Here, we present results of baseline data. Study procedures included lumbar puncture for CSF collection and 1-hour cognitive testing. CSF total Tau (T-Tau), phosphorylated Tau (P-Tau), and amyloid beta levels were determined using sandwich ELISA. Cognitive testing battery provided assessment of several cognitive domains (memory, executive, and visuospatial).

Results

Table 1. Demographic Characteristics

	African American (n=30)	White (n=50)	*p*
Age	60.1 ± 7.8	58.5 ± 6.1	0.30
Gender (% female)	83.3%	56.0%	**0.0123**
Education	10.7% High School/GED 39.3% College graduate 50.0% Post-graduate	18.0% High School/GED 38.0% College graduate 44.0% Post-graduate	0.68
Income	10.7% $19,000 or less 17.9% $20-39,000 28.6% $40-59,000 17.9% $60-79,000 25.0% $80,000 or more	12.0% $20-39,000 4.0% $40-59,000 18.0% $60-79,000 66.0% $80,000 or more	**0.0005**
Blood Pressure (systolic)	127.6 ± 13.3	125.1 ± 12.3	0.42
Blood Pressure (diastolic)	77.3 ± 7.0	77.3 ± 9.0	0.99
Hours of sleep	6.0 ± 1.1	7.2 ± 0.9	**<0.0001**
ApoE ε4 status	48.3%	50.0%	0.88

Table 2. Alzheimer's Disease Markers

	African American (n =30)	White (n=50)	*p*
β –amyloid (pg/ml)			
Triplex Aβ1-38	2029.2 ± 672.9*	2466.3 ± 760.3	**0.0268***
Triplex Aβ1-40	5020.9 ± 1312.7	5750.0 ± 1618.2	0.07
Triplex Aβ1-42	413.1 ± 107.5	419.9 ± 150.0	0.85
ELISA Aβ1-42	722.0 ± 164.2	703.7 ± 197.3	0.71
			p (Wilcoxen)
Aβ1-42/ Aβ1-40	0.1 (0.1 – 0.1)	0.1 (0.1 – 0.1)	0.08
Tau (pg/ml)			***p (Wilcoxen)***
t-tau	199.0 (166.0 – 244.0)	297.0* (228.0 – 423.0)	**0.0036***
p-tau	37.0 (34.0 – 42.0)	48.0* (37.0 – 64.0)	**0.0055***

Aβ1-42/ Aβ1-40, t-tau, and p-tau were non-parametric and necessitated use of Wilcoxen tests. Reported values for these variables are medians.

Table 3. Cognitive Testing

	African American	White	*p (Wilcoxen)*
MOCA	25.0 (24.0 – 27.0)*	27.0 (25.0 – 29.0)	**0.0051**
Trails B	81.0 (69.0 – 101)*	70.0 (56.0 – 82.0)	**0.0239**
Forwards Digit Span	6.5 (5.5 – 7.0)	7.0 (6.0 – 8.0)	0.22
Backwards Digit Span	4.0 (3.0 – 5.0)	5.0 (4.0 – 6.0)	0.10
Mental Rotation	17.5 (15.0 – 20.0)	18.5 (13.0 – 21.0)	0.50
Benson Delay	12.0 (10.0 – 14.0)	12.0 (10.0 – 13.0)	0.28
Buschke Delay	6.0 (2.0 – 8.0)*	7.0 (5.0 – 9.0)	**0.0218**
MINT	29.0 (28.0 – 31.0)*	31.0 (30.0 – 32.0)	**0.0017**

Reported values are medians.

Table 1 shows that participants are middle-aged, have a college or postgraduate degree, and health-range blood pressure, half of participants were positive for ApoE4. AAs reported less sleep than Whites.

Table 2 and Figure 1 show results of AD biomarker levels in AAs and Whites. AAs had significantly less T-Tau, P-Tau, and Aβ1–38.

Table 3 shows results of Cognitive testing in AAs and Whites. AAs performed more poorly than Whites on all tests, and significantly on tests of executive function, global cognition, verbal memory and language.

Figure 2 and Figure 3 show results of polynomial regression analysis which found that after adjustment for age, gender, education, and ApoE4 status, race significantly modified the relationship between T-Tau, P-Tau, and executive function.

Figure 1. Comparison of Total Tau and Phosphorylated Tau between African Americans and Whites

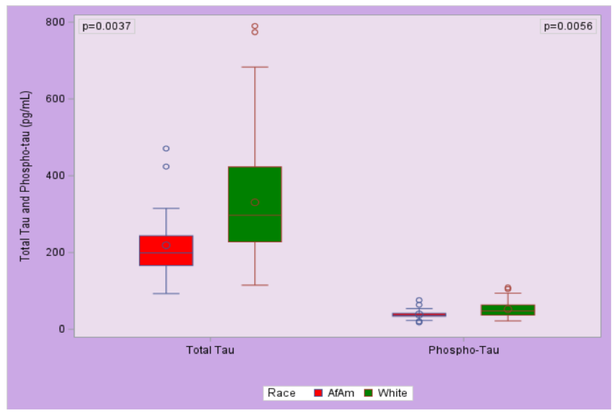


Figure 2. Relationship between Trail B and Total Tau in African Americans and Whites

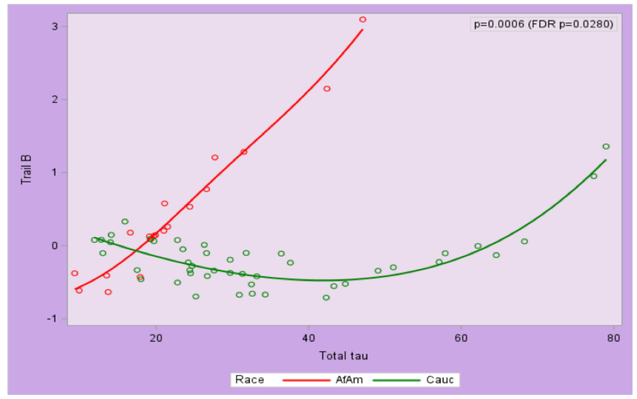
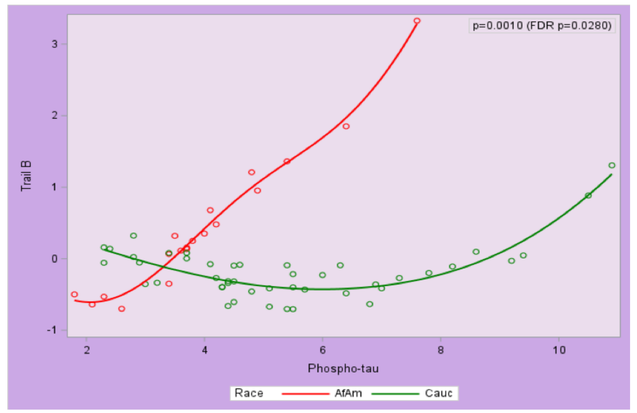


Figure 3. Relationship between Trail B and Phosphorylated Tau in African Americans and Whites



Conclusions

In a cohort of healthy middle-aged individuals with a parental history of AD, **AAs had lower total Tau and phosphorylated Tau burden than Whites**. Even when controlled for blood pressure and demographic risk factors, **race significantly modified the relationship between T-Tau, P-Tau, and executive functions.** Smaller increases in Tau were related to poorer cognition for AAs versus Whites. Results suggest that existing cutoff values for CSF biomarkers may not be appropriate for AAs, and should be adjusted for race.

Future Research

This is the first study to show that AAs and Whites may have different cutoffs for AD CSF biomarkers. It is possible that AAs are sensitive to smaller changes in Tau compared to Whites. Importantly, since we focused on the baseline data of the ASCEND study, we did not look at individuals over time. Therefore, we cannot draw a true correlation between increasing Tau and poorer cognition.

References

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Acknowledgements

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