The Effect of Inflammatory Biomarker Levels and Physiological Stress Indices on High-Risk Individuals of Alzheimer's Disease

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Purpose

With more kills than breast cancer and prostate cancer combined, Alzheimer's disease (AD) is the sixth leading cause of death in the United States. Additionally, individuals with a parental history of AD have ten times the risk to become afflicted with AD, and African-Americans have twice the risk of developing AD than Caucasians[1]. This neurodegenerative disease, caused by beta-amyloid plaques and tau protein tangles[2], is negatively impacting the lives of millions today. To combat the increasing incidence of AD, it is important to focus prevention efforts in individuals at high risk, including AD family caregivers. Stress and inflammatory markers associated with AD caregiving not only negatively impact physical health, but are also independent risk factors for AD[4]. The focus of this study is to investigate the relationship between blood and cerebrospinal fluid (CSF) biomarkers of stress and inflammation in correlation with AD biomarkers in African-American and Caucasian family caregivers of AD patients.

Participants/Methods

Participants include Caucasian and African-American adults (45 or older) with parental history of AD. Individuals with any significant neurologic disease, major depression within the last two years, history of alcohol or substance abuse, or history of mental health illnesses were excluded from the study. All participants were enrolled in and consented for the NIH funded study, ASCEND.

Inflammation

Participants were asked to fast overnight prior to their visit to the Emory Brain Health Center. Around 45 mL of blood and 20 mL of CSF were collected via a blood draw and a lumbar puncture (LP) by a trained professional in a designated clinical room. After collection and storage, blood and CSF biomarker levels were analyzed via assays.

Results

Table 1: Participant Demographics of Caucasian and African-American Individuals

	Caucasian (n = 45)	African-American (n = 29)
Age	58.53 +/- 6.18	59.41 +/- 8.12
Sex	Female: 57.8%*	Female: 86.2%*
Level of Education	HS/GED: 17.8% College grad: 35.6% Postgrad: 46.7%	HS/GED: 10.3% College grad: 41.4% Postgrad: 48.3%
BMI	26.45 +/- 5.04	28.33 +/- 5.52
Blood Pressure	125.79 +/- 12.58 / 77.74 +/- 9.48	129.00 +/- 13.49 / 77.74 +/- 6.84

Table 3: Correlational Data of CSF vs AD Biomarkers

	Tau	P-Tau	Aβ -38	Aβ -40	Aβ -42
MMP-1	.196	.205	.243*	.172	.102
(n = 20) AA	*-.030*	*.044*	*.057*	*-.043*	*.097*
(n = 42) CC	*.246*	*.242*	*.334***	*.261*	*.154*
MMP-2	.215	.237	.373**	.365*	.338**
AA	*.679***	*.669***	*.799***	*.741***	*.512**
CC	*.038*	*.047*	*.128*	*.178*	*.254*
IL-7	.016	.025	.025	.019	.061
AA	*.593***	*.569***	*.452**	*.351*	*.071*
CC	*-.221*	*-.213*	*-.199*	*-.143*	*.092*
IL-8	.143	.153	.268*	.348**	.274*
AA	*.409*	*.379*	*.457**	*.550**	*.323*
CC	*.178*	*.167*	*.221*	*.285*	*.175*
IL-9	.298*	.345**	.509**	.416**	.346**
AA	*.469**	*.470**	*.561**	*.484**	*.186*
CC	*.283*	*.333**	*.497***	*.384**	*.474***
MCP-1	.109	.138	.205	.206	.221
AA	*.454**	*.502**	*.526**	*.528**	*.360*
CC	*.199*	*.209*	*.241*	*.213*	*.200*
TGFA	.342**	.371**	.477**	.423**	.344**
AA	*.346*	*.390*	*.522**	*.429*	*.356*
CC	*.412***	*.420***	*.508***	*.449***	*.346**
ICAM-1	.358**	.383**	.432**	.343**	.154
AA	*.455**	*.414*	*.523**	*.523**	*.246*
CC	*.419***	*.454***	*.472***	*.330**	*.159*
VCAM-1	.592**	.595**	.604**	.684**	.365**
AA	*.671***	*.646***	*.580***	*.558**	*.119*
CC	*.526***	*.534***	*.584***	*.724***	*.464***

Table 2: Biomarker Data Differentiated by Race

	Caucasian	African-American
Plasma	**(n = 43)**	**(n = 25)**
IL-7	4.99 +/- 2.45	6.56 +/- 4.26
IL-8	25.12 +/- 33.19	14.22 +/- 15.41
IL-9	1.76 +/- 2.10	3.01 +/- 7.22
IL-10	11.16 +/- 5.88	11.39 +/- 10.43
MCP-1	180.50 +/- 73.60**	234.21 +/- 71.85**
MDC	931.50 +/- 396.73*	1172.94 +/- 344.61*
TGFA	4.12 +/- 7.87	7.78 +/- 21.86
TNFA	7.65 +/- 6.38	7.66 +/- 3.93
IFNG	37.34 +/- 125.32	32.17 +/- 77.57
ICAM-1	562.92 +/- 308.48	520.23 +/- 111.61
VCAM-1	4436.02 +/- 2546.88	3568.42 +/- 889.60
CRP (µg/ml)	4.77 +/- 4.99**	15.12 +/- 19.23**
SAP (µg/ml)	10.01 +/- 3.02*	12.05 +/- 3.43*
CSF	**(n = 42)**	**(n = 20)**
MMP-1	7.83 +/- 5.73	7.26 +/- 5.77
MMP-2	20667.81 +/- 4607.06	18314.17 +/- 4703.35
MMP-9	12.75 +/- 8.04	17.40 +/- 16.71
IL-7	1.85 +/- 0.84**	1.28 +/- 0.59**
IL-8	72.40 +/- 23.79	78.67 +/- 16.91
IL-9	3.72 +/- 1.78	3.02 +/- 2.07
IL-10	5.68 +/- 2.37	5.85 +/- 3.12
MCP-1	5459.43 +/- 572.21*	5787.30 +/- 338.21*
MDC	109.42 +/- 58.55	126.12 +/- 83.31
TGFA	8.62 +/- 2.38	8.95 +/- 2.09
ICAM-1	291.82 +/- 160.23	320.64 +/- 180.42
VCAM-1	27.55 +/- 11.29**	19.16 +/- 7.70**
AD	**(n = 43)**	**(n = 20)**
Tau	335.51 +/- 179.90**	218.65 +/- 96.39**
P-Tau	52.98 +/- 22.42*	39.10 +/- 14.12*
Aβ -38	2431.44 +/- 784.66*	2015.50 +/- 687.39*
Aβ -40	5657.49 +/- 1655.84	5012.70 +/- 1346.25
Aβ -42	406.21 +/- 144.47	406.15 +/- 105.28

Table 1 shows that while there were more female participants, the average participant demographic is middle aged, has a college or postgraduate degree, and has relatively normal BMI and blood pressure levels.

Table 2 shows results of plasma, CSF, and AD biomarker levels (measured in pg/ml) in Caucasians vs. African-Americans. Significant correlations were seen in plasma MCP-1, MDC, CRP, and SAP; in CSF IL-7, MCP-1, and VCAM-1; and in AD Tau, P-Tau, and Aβ-38.

Table 3 shows Pearson's R correlational data between CSF and AD biomarkers in Caucasians (CC) vs. African-Americans (AA). Many significances were seen, more often with AA's (CC's more often significant for TGFA, ICAM-1, and VCAM-1). No significant correlations were found between plasma biomarkers and AD biomarkers of the sample.

All correlations were done using Pearson's R correlations to assess the statistical difference between racial groups.

*Significant correlation where p < 0.05
**Significant correlation where p < 0.01

Conclusion

- Biomarkers in blood plasma and CSF do show significant differences across races, thus race may factor into the difference of peripheral and central indications of inflammation leading to AD
- CSF biomarkers were more significantly associated with AD biomarkers than with blood plasma biomarkers, especially in the African-American population

Future Directions

- Further biomarker-specific research: deepen our understanding of the differentiated association of inflammation and AD
- Further intervention-specific research: observe changes in these biomarkers in response to drugs and exercise/diet
- Clinical applicability: allow blood draws or LP's to be routinely practiced for at-risk individuals of AD in the clinical setting

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