Subjective and Biological Markers of Stress in Middle-Aged Caucasian and African American Alzheimer's Disease Families

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Introduction

Recognition of family caregiving in AD is receiving much attention. Both depression and stress are linked to caregiving and are themselves independent risk factors for AD.[1] Caucasian (CC) family caregivers are often spouses of AD patients, whereas African American (AA) caregivers are often adult women children of AD patients.[2] Perceptions regarding AD caregiving may differ by race, such that AAs may be less likely than CCs to report caregiver-related stress,[3] despite the fact that AA non-AD caregivers report more stress and depression than CCs. This phenomenon is important to investigate physiologically, because middle-aged, female, AA family caregivers are at risk for hypertension and diabetes, which are potentially exacerbated by caregiver stress. In this study, we investigated the extent to which subjective and biological markers of stress in both blood and cerebrospinal fluid (CSF) differ by race among middle-aged AD family caregivers.

Methods

Participants were middle-aged AAs and CCs with a parental history of AD defined by NINDS-ADRDA criteria. Study visits included vital signs collection, blood and CSF collection via a blood draw and a lumbar puncture, and 1.5-hour battery of 7 standardized caregiver stress questionnaires. CSF samples were collected after an 8-hour overnight fast and followed the guidelines in the "NIA Biospecimens Best Practice Guidelines for the ADCs". 3 panels of plasma and CSF biomarkers were measured including cytokines and chemokines, C-reactive protein, and endothelial markers. A battery of 7 stress measures, assessing the positive and negative aspects of caregiving, includes CES-D, DEMQOL, Pearlin Caregivers' Stress Scale, Perceived Stress Scale, QoL-AD, Zarit Burden Interview and PHQ-8. We controlled for age, sex, education, ApoE4 status, and blood pressure. All tests were two-tailed and alpha values were set at 0.05.

Results

Table 1. Sample Characteristics

	African American, n=30	Caucasian, n=50	p Value
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 50.5% Post-Graduate	18.0% High School/GED 38.0% College Graduate 44.0% Post-Graduate	0.68
APOE ε4 Status	48.3%	50.0%	0.88
Systolic Blood Pressure	127.6 ± 13.3	125.1 ± 12.3	0.42

Table 2. Comparison of Inflammatory Biomarkers between AAs and CCs

	African American, n=30 Median (IQR)	Caucasian, n=50 Median (IQR)	p Value
Plasma Inflammatory Markers, pg/mL			
IL-7	6.1 (3.9 – 9.7)	4.7 (2.8 – 6.2)	0.0249
IL-8	6.2 (4.4 – 17.1)	9.9 (5.2 – 31.6)	0.10
IL-9	1.7 (1.1 – 3.2)	1.3 (0.7 – 2.6)	0.28
IL-10	8.5 (6.8 – 14.1)	10.5 (7.7 – 14.3)	0.53
MCP-1	213 (186 – 259)	164 (138 – 203)	0.0011
MDC	1071 (876 – 1441)	854 (689 – 1152)	0.0046
TGF-α	2.3 (1.3 – 4.4)	1.6 (0.9 – 3.9)	0.46
TNF-α	7.8 (5.4 – 10.1)	5.5 (4.7 – 7.6)	0.10
Interferon-γ	12.6 (7.7 – 20.4)	10.3 (4.5 – 19.7)	0.63
ICAM-1	532 (430 – 631)	516 (462 – 633)	0.82
VCAM-1	3442 (3045 – 4002)	3930 (3482 – 4782)	0.0051
CRP, µg/mL	13.3 (5.1 – 20.5)	3.3 (1.5 – 6.9)	0.0008
SAP, µg/mL	12.0 (10.1 – 13.2)	9.9 (8.3 – 12.5)	0.0419
CSF Inflammatory Markers, pg/mL			
MMP-1	5.7 (4.1 – 7.7)	6.6 (4.9 – 8.6)	0.22
MMP-2	17645 (14621 – 21356)	20657 (17766 – 23490)	0.0256
MMP-9	12.8 (7.4 – 24.5)	11.6 (5.9 – 18.1)	0.34
IL-7	1.3 (0.8 – 1.6)	1.7 (1.3 – 2.4)	0.0046
IL-8	71.3 (63.4 – 90.6)	69.4 (57.3 – 88.2)	0.37
IL-9	3.2 (1.5 – 4.0)	3.9 (2.3 – 5.3)	0.13
IL-10	6.1 (3.9 – 8.0)	5.4 (4.1 – 6.7)	0.55
MCP-1	5579 (5505 – 5931)	5590 (5375 -5838)	0.06
MDC	88.3 (67.4 – 188)	99.5 (69.2 – 144)	0.97
TGF-α	8.9 (7.3 – 9.8)	9.1 (7.1 – 9.5)	0.70
TNF-α	1.2 (1.0 – 1.9)	1.1 (0.6 – 1.5)	0.28
TIMP-1	35.5 (31.1 – 42.1)	36.2 (31.3 – 42.1)	0.70
TIMP-2	37.9 (33.5 – 45.3)	41.4 (36.8 – 47.2)	0.12
ICAM-1	301 (188 – 402)	243 (183 – 337)	0.34
VCAM-1	19.8 (13.6 – 23.8)	26.0 (18.8 – 34.0)	0.0056

Results

30 AAs and 50 CCs were consented and enrolled in the study. 28 participants were currently caregivers and 48 were past caregivers for their parent, now deceased. Participants were middle-aged (59.1) and well-educated (85% completed college). 83.3% of AAs were female compared with 56.0% of CCs. 49.4% of participants were ApoE ε4 positive, consistent with prior studies of AD family history. Systolic blood pressure (126.4 mmHg) suggests an overall healthy sample that did not differ by race. Participants reported moderate levels of stress and depression, with no differences between AAs and CCs among any of the 7 self-reported stress questionnaires. AAs had higher levels of 10 of 13 stress biomarkers in plasma, with significantly higher values of IL-7, MCP, MDC, CRP, and SAP. On the other hand, CCs have higher levels of 9 of 15 stress biomarkers in CSF, with significantly higher values of MMP-2, IL-7, and VCAM-1.

Summary and Conclusions

While AAs and CCs self-reported similar levels of caregiver stress, AAs have significantly higher biological indices of stress in blood than CCs. This discrepancy between races in plasma is reversed in CSF inflammatory markers, therefore indicating that peripheral inflammation does not necessarily map onto inflammation in the central nervous system. Results suggest that there is a discrepancy in the subjective and biological measures of stress among middle-aged adult caregivers and that this discrepancy differs by race.

Future Research

Future Studies should assess the role of subjective stress among AAs as a potential cause of increased inflammation and how role resilience and dementia stigma may influence these biomarker differences.

References

1. Pinquart, M., & Sörensen, S. (2003). Differences between caregivers and noncaregivers in psychological health and physical health: A meta-analysis. *Psychology and Aging, 18*(2), 250-267. doi:10.1037/0882-7974.18.2.250
2. Pinquart, M., & Sörensen, S. (2005). Ethnic Differences in Stressors, Resources, and Psychological Outcomes of Family Caregiving: A Meta-Analysis. *The Gerontologist, 45*(1), 90-106. doi:10.1093/geront/45.1.90 %J The Gerontologist
3. Rajagopal, D., Brody, E., Lawton, M. P., & Kleban, M. H. (1992). The Dynamics of Caregiving for a Demented Elder Among Black and White Families. *Journal of Gerontology, 47*(4), S156-S164. doi:10.1093/geronj/47.4.S156 %J Journal of Gerontology

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