Inflammatory Biomarkers in the Texas Alzheimer's Research Consortium (TARC) Cohort

Rachelle Doody[1], Wenyaw Chan[1], Robert Barber[4], Christie Ballantyne[1], Valory Pavlik[1], Sid O'Bryant[3], Eveleen Darby[1], Ramon Diaz-Arrastia[2], Thomas Fairchild[4], Donald Royall[5], Perrie Adams[2], and the TARC Investigators

Background

- AD has been linked to a state of local and system inflammation and altered expression of both pro- and anti-inflammatory markers.
- Prospective studies show an increased AD risk associated with inflammatory proteins in serum.
- A heightened inflammatory state may mediate the relationship between prevalent cardiovascular disease (CVD) and AD.

Hypotheses

- TARC participants with probable AD will have a significantly different inflammatory profile than non-demented controls
- Prevalent CVD will account for some of the relationship between case-control status and inflammatory marker profile

Methods

- Participants were 197 AD cases and 198 normal controls enrolled in the TARC cohort and examined using standardized procedures.
- Diagnosis of AD status was based on NINCDS-ADRDA criteria and controls performed within normal limits on psychometric assessment.
- Inflammatory markers were quantified in serum using a multiplexed immunoassay human Multi-Analyte Profile (humanMAP) developed by Rules Based Medicine (rulesbasedmedicine.com).
- After inspection of distributions, inflammatory biomarkers were dichotomized at the median, except for TNF-alpha, dichotomized at the 10th percentile.
- CVD and CVD equivalent (CVDE) classified according to Adult Treatment Panel III guidelines (see Table 1).
- Fischer's exact test (unadjusted) and logistic regression analysis (adjusted) used to assess the association of inflammatory marker level with case-control status, and the interaction of CVDE with inflammatory markers.
- Models were adjusted for age, sex, and BMI.

Results

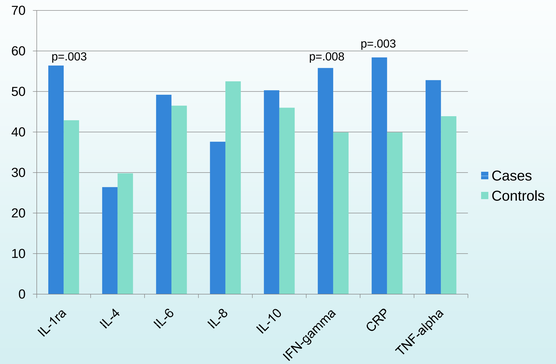
- Cases were older and had lower BMI (see Table 1).
- CVDE prevalence was similar in the two groups.
- Three inflammatory markers were significantly (unadjusted and adjusted) lower in cases than controls: IL-1ra, IFN-gamma and CRP.
- No interaction between CVDE and any biomarker in predicting case-control status.

Table 1. Characteristics of Cases and Controls

	AD Cases (n=197)	Controls (n=198)	p
	Mean (±SD) or Percent	Mean (±SD) or Percent	
Covariates			
Age at Visit	77.41 (8.29)	70.42 (8.89)	**<.001**
Sex (% female)	34.52	31.82	.750
BMI (kilos/meters²)	25.68 (5.06)	27.48 (4.82)	**<.001**
CVD Equivalent*	48.22	46.46	.726
MMSE	19.18 (6.22)	29.42 (0.88)	**<.001**
Inflammatory Biomarkers			
IL1ra (pg/mL)	109.3(61.1)	134.9(75.6)	**<.001**
IL-1beta (pg/mL)	Below detectable limits	Below detectable limits	
IL-4 (pg/mL)	13.0(13.5)	11.7(15.9)	.43
IL-6 (pg/mL)	4.21(30.6)	1.69 (1.84)	.25
IL-8 pg/mL)	24.0 (8.19)	21.9 (9.38)	**.01**
IL-10 (pg/mL)	9.16 (5.32)	10.95 (6.88)	**.004**
IFN-gamma (pg/mL)	3.09 (6.87)	3.03 (1.98)	.89
C Reactive Protein (ug/mL)	3.23 (4.87)	3.68 (4.14)	.32
TNF-alpha pg/mL)	4.74 (3.60)	6.33 (5.44)	**.001**

*Calculated according to Adult Treatment Panel III guidelines (history of MI, stent placement, CHF, Diabetes, or any two of HTN, hyperlipidemia, or current smoking)

Proportion of Cases and Controls *Below* the Median for Each Biomarker



Note: p-values are for odds ratios from models adjusted for age, sex, and BMI. No other contrasts significant after adjustment. p-values for all CVDE * biomarker interaction terms >.05.

Conclusion

- Inflammatory biomarkers are not elevated in established AD cases relative to healthy controls.
- Inflammatory profiles are characterized by lower levels of some inflammatory markers in AD cases.
- CVD and its risk factors did not influence the inflammatory profile of either group.
- Although we adjusted for BMI, the reduced inflammatory markers in AD cases could be related to mechanisms that lead to weight loss in AD.

TARC Consortium Members: [1]Baylor College of Medicine, [2]UT-Southwestern Medical Center, [3]Texas Tech Health Sciences Center, [4]University of North Texas Health Science Center, [5]UT Health Science Center—San Antonio