A screenshot of a cell phone

Description automatically generated**Figure e-1. Racial differences in CSF sTREM2 levels in the Alzheimer Disease Neuroimaging Initiative cohort.** The natural logarithm of CSF concentrations of soluble triggering receptor expressed on myeloid cells 2 (sTREM2) were plotted as a function of *TREM2* coding variant (**A**), *MS4A4A* rs1582763 genotype (**B**), or *TREM2* coding variant status and *MS4A4A* rs1582763 (A) carrier status (**C**). For all plots, the corresponding sTREM2 concentrations in pg/ml are shown on the right axis. Red squares represent samples from AA, and grey circles represent samples from NHW. Horizontal dashed lines indicate the mean sTREM2 levels for AA (red) and NHW (grey) groups. Vertical dotted lines separate genetic groups. The number of individuals in each group is listed (n).

**eTable-1. Model for CSF Elecsys Aβ42 concentrations.**

The natural logarithm-transformed concentration of CSF Elecsys Aβ42 was the outcome variable in an analysis of covariance (ANCOVA) model with the following predictor variables: race (African American [AA] or non-Hispanic white [NHW]), centered age (the age at CSF collection minus the mean age for the cohort [69.0 years]), sex, years of education (≤12 and >12 years of education), family history of dementia (positive or negative), *APOE* ε4 status (ε4 carrier or non-carrier), dementia status (CDR=0 or CDR>0), and every two way interaction among these variables. Factors not shown were not significant.

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| **Covariate** | **Category** | **log(Aβ42)** | **p=** |
| Race | AA  NHW | 6.79 (0.08)  6.92 (0.03) | 0.10 |
| Age (years) |  | -0.01 (0.01) | N.S. |
| Dementia status | CDR=0  CDR>0 | 7.00 (0.04)  6.70 (0.07) | 0.0003 |
| Dementia status x age  (intercept) | CDR=0  CDR>0 | 6.99 (0.04)  6.70 (0.07) | 0.0004 |
| Dementia status x age  (slope) | CDR=0  CDR>0 | -0.01 (0.004)  -0.002 (0.01) | N.S. |
| *APOE* ε4 | Positive  Negative | 7.04 (0.05)  6.67 (0.07) | <0.0001 |
| Sex | Male  Female | 6.73 (0.05)  6.98 (0.05) | 0.0003 |
| Sex x race | AA Male  NHW Male  AA Female  NHW Female | 6.59 (0.10)  6.87 (0.04)  6.98 (0.10)  6.97 (0.03) | 0.02  N.S. |

Abbreviations: AA, African American; Aβ42, amyloid-β 42; CDR, Clinical Dementia Rating where CDR=0 indicates cognitive normality and CDR>0 indicates dementia; CSF, cerebrospinal fluid; NHW, non-Hispanic white, N.S., not significant.

**eTable-2. Model for CSF Elecsys tTau concentrations.**

The natural logarithm-transformed concentration of CSF Elecsys tTau was the outcome variable in an analysis of covariance (ANCOVA) model with the following predictor variables: race (African American [AA] or non-Hispanic white [NHW]), centered age (the age at CSF collection minus the mean age for the cohort [69.0 years]), sex, years of education (≤12 and >12 years of education), family history of dementia (positive or negative), *APOE* ε4 status (ε4 carrier or non-carrier), dementia status (CDR=0 or CDR>0), and every two way interaction among these variables. Factors not shown were not significant.

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| **Covariate** | **Category** | **log(tTau)** | **p=** |
| Race | AA  NHW | 5.21 (0.07)  5.54 (0.02) | <0.0001 |
| Age (years) |  | -0.001 (0.005) | 0.03 |
| Dementia status | CDR=0  CDR>0 | 5.25 (0.03)  5.51 (0.06) | 0.0002 |
| Dementia status x age  (intercept) | CDR=0  CDR>0 | 5.26 (0.03)  5.51 (0.06) | 0.0003 |
| Dementia status x age  (slope) | CDR=0  CDR>0 | 0.010 (0.003)  0.002 (0.005) | 0.01 |
| Sex | Male  Female | 5.31 (0.05)  5.45 (0.05) | 0.02 |
| Sex x race | AA Male  NHW Male  AA Female  NHW Female | 5.09 (0.08)  5.53 (0.04)  5.34 (0.08)  5.55 (0.03) | <0.0001  0.06 |

Abbreviations: AA, African American; CDR, Clinical Dementia Rating where CDR=0 indicates cognitive normality and CDR>0 indicates dementia; CSF, cerebrospinal fluid; NHW, non-Hispanic white; tTau, total tau.

**eTable-3. Model for CSF Elecsys pTau concentrations.**

The natural logarithm-transformed concentration of CSF Elecsys pTau was the outcome variable in an analysis of covariance (ANCOVA) model with the following predictor variables: race (African American [AA] or non-Hispanic white [NHW]), centered age (the age at CSF collection minus the mean age for the cohort [69.0 years]), sex, years of education (≤12 and >12 years of education), family history of dementia (positive or negative), *APOE* ε4 status (ε4 carrier or non-carrier), dementia status (CDR=0 or CDR>0), and every two way interaction among these variables. Factors not shown were not significant.

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| **Covariate** | **Category** | **log(pTau)** | **p=** |
| Race | AA  NHW | 2.83 (0.07)  3.16 (0.03) | <0.0001 |
| Age (years) |  | 0.001 (0.005) | 0.04 |
| Dementia status | CDR=0  CDR>0 | 2.86 (0.04)  3.13 (0.07) | 0.0003 |
| Dementia status x age  (intercept) | CDR=0  CDR>0 | 2.87 (0.04)  3.14 (0.07) | 0.0004 |
| Dementia status x age  (slope) | CDR=0  CDR>0 | 0.010 (0.004)  0.002 (0.005) | 0.02 |
| Sex | Male  Female | 2.94 (0.05)  3.05 (0.05) | 0.08 |
| Sex x race | AA Male  NHW Male  AA Female  NHW Female | 2.72 (0.09)  3.16 (0.04)  2.94 (0.09)  3.16 (0.03) | <0.0001  N.S. |

Abbreviations: AA, African American; CDR, Clinical Dementia Rating where CDR=0 indicates cognitive normality and CDR>0 indicates dementia; CSF, cerebrospinal fluid; NHW, non-Hispanic white; N.S., not significant; pTau, phosphorylated tau181.

**eTable-4. Model for CSF NfL concentrations.**

The natural logarithm-transformed concentration of CSF NfL was the outcome variable in an analysis of covariance (ANCOVA) model with the following predictor variables: race (African American [AA] or non-Hispanic white [NHW]), centered age (the age at CSF collection minus the mean age for the cohort [69.0 years]), sex, years of education (≤12 and >12 years of education), family history of dementia (positive or negative), *APOE* ε4 status (ε4 carrier or non-carrier), dementia status (CDR=0 or CDR>0), and every two way interaction among these variables. Factors not shown were not significant.

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| **Covariate** | **Category** | **log(NfL)** | **p=** |
| Race | AA  NHW | 7.25 (0.06)  7.47 (0.02) | 0.0005 |
| Age (years) |  | 0.02 (0.005) | <0.0001 |
| Dementia status | CDR=0  CDR>0 | 7.23 (0.03)  7.49 (0.06) | <0.0001 |
| Dementia status x age  (intercept) | CDR=0  CDR>0 | 7.26 (0.03)  7.51 (0.06) | 0.0001 |
| Dementia status x age  (slope) | CDR=0  CDR>0 | 0.03 (0.003)  0.02 (0.005) | 0.01 |

Abbreviations: AA, African American; CDR, Clinical Dementia Rating where CDR=0 indicates cognitive normality and CDR>0 indicates dementia; CSF, cerebrospinal fluid; NfL, neurofilament light chain; NHW, non-Hispanic white.

**eTable-5. Model for CSF sTREM2 concentrations.**

The natural logarithm-transformed concentration of CSF sTREM2 was the outcome variable in an analysis of covariance (ANCOVA) model with the following predictor variables: race (African American [AA] or non-Hispanic white [NHW]), centered age (the age at CSF collection minus the mean age for the cohort [69.0 years]), sex, years of education (≤12 and >12 years of education), family history of dementia (positive or negative), *APOE* ε4 status (ε4 carrier or non-carrier), dementia status (CDR=0 or CDR>0), and every two way interaction among these variables. Factors not shown were not significant.

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| **Covariate** | **Category** | **log(sTREM2)** | **p=** |
| Race | AA  NHW | 7.21 (0.05)  7.52 (0.02) | <0.0001 |
| Age (years) |  | 0.01 (0.004) | <0.0001 |
| Dementia status | CDR=0  CDR>0 | 7.31 (0.03)  7.43 (0.05) | 0.04 |
| Dementia status x age  (intercept) | CDR=0  CDR>0 | 7.32 (0.03)  7.44 (0.05) | 0.04 |
| Dementia status x age  (slope) | CDR=0  CDR>0 | 0.01 (0.003)  0.01 (0.004) | N.S. |

Abbreviations: AA, African American; CDR, Clinical Dementia Rating where CDR=0 indicates cognitive normality and CDR>0 indicates dementia; CSF, cerebrospinal fluid; NHW, non-Hispanic white; N.S., not significant; sTREM2, soluble triggering receptor expressed on myeloid cells 2.

**eTable-6. Characteristics of Knight Alzheimer Disease Research Center sub-cohort with each African American matched with a non-Hispanic white participant.** A computer algorithm matched each African American (AA) participant, if possible, with a non-Hispanic white (NHW) participant by age (within three years), years of education (within two years), dementia status (CDR=0 or CDR>0), and family history of AD. If more than one NHW participant match was available, the participant with the closest age was chosen. A NHW participant with matching covariates was found for 86 of 91 AA participants. Continuous measures are presented as the mean ± standard deviation. The significance of differences between groups was determined by paired t-tests for continuous variables and by Chi-Square tests for categorical variables.

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|  | **African American Participants** | | **Non-Hispanic White Participants** | |  |
| **Characteristic** | **n=** |  | **n=** |  | **p=** |
| Age at CSF collection (years) | 86 | 66.0 ± 8.0 | 86 | 66.0 ± 8.1 | N.S. |
| Sex (n, % Female) | 86 | 46, 53% | 86 | 45, 52% | N.S. |
| Years of education | 86 | 15.5 ± 2.6 | 86 | 15.5 ± 2.6 | N.S. |
| *APOE* ε4 status (n, % carrier) | 85 | 35, 41% | 86 | 31, 36% | N.S. |
| CDR 0/0.5/1 (% >0) | 86 | 75/8/3 (13%) | 86 | 75/8/3 (13%) | N.S. |
| Family history (n % positive) | 86 | 36, 42% | 86 | 36, 42% | N.S. |
| **Unadjusted raw values (± standard deviation)** | | | | | |
| Elecsys CSF Aβ42 (pg/ml) | 77 | 1308 ± 700 | 72 | 1482 ± 663 | 0.05 |
| Elecsys CSF tTau (pg/ml) | 77 | 182 ± 77 | 72 | 247 ± 120 | <0.0001 |
| Elecsys CSF pTau (pg/ml) | 77 | 16.5 ± 7.3 | 72 | 23.0 ± 13.6 | 0.0001 |
| CSF NFL (pg/ml) | 85 | 1342 ± 731 | 85 | 1517 ± 922 | 0.03 |
| CSF sTREM2 (pg/ml) | 86 | 1337 ± 463 | 86 | 1756 ± 470 | <0.0001 |
| **Unadjusted natural logarithm transformed values (± standard deviation)** | | | | | |
| Elecsys CSF Aβ42 (pg/ml) | 77 | 7.04 ± 0.54 | 72 | 7.19 ± 0.52 | 0.05 |
| Elecsys CSF tTau (pg/ml) | 77 | 5.13 ± 0.39 | 72 | 5.42 ± 0.42 | <0.0001 |
| Elecsys CSF pTau (pg/ml) | 77 | 2.73 ± 0.38 | 72 | 3.01 ± 0.47 | <0.0001 |
| CSF NFL (pg/ml) | 85 | 7.09 ± 0.47 | 85 | 7.21 ± 0.44 | 0.05 |
| CSF sTREM2 (pg/ml) | 86 | 7.13 ± 0.39 | 86 | 7.43 ± 0.29 | <0.0001 |

Abbreviations: Aβ42, amyloid-β 42; CDR, Clinical Dementia Rating where CDR=0 indicates cognitive normality and CDR=0.5, 1, 2, or 3 indicates very mild, mild, moderate, or severe dementia, respectively; CSF, cerebrospinal fluid; NFL, neurofilament light protein; N.S., not significant; pTau, phosphorylated tau181; sTREM2, soluble triggering receptor expressed on myeloid cells 2; tTau, total tau.

**eTable-7. Model for CSF sTREM2 concentrations including genetic variants.**

The natural logarithm-transformed concentration of CSF sTREM2 was the outcome variable in an analysis of covariance (ANCOVA) model with the following predictor variables: race (African American [AA] or non-Hispanic white [NHW]), centered age (the age at CSF collection minus the mean age for the cohort [69.0 years]), sex, years of education (≤12 and >12 years of education), family history of dementia (positive or negative), *APOE* ε4 status (ε4 carrier or non-carrier), dementia status (CDR=0 or CDR>0), *TREM2* variant carrier status, rs1582763 minor allele carrier status, and every two way interaction among these variables. The interaction between *TREM2* variant carrier status and rs1582763 minor allele carrier status was not significant. The interaction between race and family history and the interaction between sex and education were significant (0.02 and 0.01, respectively). Factors not shown were not significant.

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| **Covariate** | **Category** | **log(sTREM2)** | **p=** |
| Race | NHW  AA | 7.43 (0.04)  7.40 (0.09) | 0.77 |
| *TREM2* coding variant status | Non-carrier  Carrier | 7.51 (0.04)  7.32 (0.07) | 0.006 |
| rs1582763 (A) | Non-carrier  Carrier | 7.26 (0.05)  7.57 (0.08) | 0.0002 |
| Age (years) |  | 0.01 (0.004) | <0.0001 |
| Dementia status | CDR=0  CDR>0 | 7.35 (0.04)  7.48 (0.07) | 0.04 |
| Race x family history | AA positive  AA negative  NHW positive  NHW negative | 7.31 (0.09)  7.49 (0.11)  7.45 (0.04)  7.42 (0.05) | N.S.  N.S. |
| Sex x education | Male ≤12 years  Male >12 years  Female ≤12 years  Female >12 years | 7.50 (0.07)  7.37 (0.05)  7.38 (0.07)  7.42 (0.06) | N.S.  N.S. |

Abbreviations: AA, African American; CDR, Clinical Dementia Rating where CDR=0 indicates cognitive normality and CDR>0 indicates dementia; CSF, cerebrospinal fluid; NHW, non-Hispanic white; N.S., not significant; sTREM2, soluble triggering receptor expressed on myeloid cells 2.