Integrating Imaging, Biomarkers, and Environmental Data to Assess Alzheimer's Disease Progression Across Diverse Populations

Tia Warrick, DHSc, MPH; Khushi R. Kanani; Prevena Ramakrishnan; Manali Misra; Snabu Neupane; Kaitlynn N. Balmer-Brown
Juniata College; Huntingdon, PA

Introduction

- Alzheimer's disease (AD) is a progressive neurodegenerative disorder influenced by genetic, environmental, and biological factors. Understanding these interactions is critical for early detection and intervention.
- Imaging, biomarkers, and environmental exposures provide complementary insights into AD progression, helping to identify at-risk populations and potential intervention targets.
- This study uniquely integrates neuroimaging, biomarker profiles, and environmental risk data to assess their combined effects on cognitive decline across diverse populations, an area with limited research.

Methods

- ADNI cohort data (ADNI1–ADNI4) was extracted, cleaned, combined, and recoded for analysis, including cognitive, biomarker, sociodemographic, and environmental risk data.
- Cognitive assessments (MMSE, ADAS-Cog, MoCA, CDR, NTB) measure memory, executive function, and disease severity. Sociodemographic factors (age, gender, ethnicity, education, home type) assess disparities in AD risk.
- Biomarkers (MRI hippocampal atrophy, PET amyloid/tau, CSF amyloid-β/tau, and NFL) track neurodegeneration, while environmental risk factors (RSEI, occupational exposure, home type) assess external contributions to AD progression.
- Statistical analyses included linear regression, interaction models, and ANOVA to assess relationships between environmental risk, biomarkers, and cognitive decline.

Conclusion

- Higher environmental exposure is associated with increased amyloid accumulation, as evidenced by lower CSF Amyloid-β ($p < 0.001$) and higher PET Amyloid SUVR ($p < 0.001$), though no significant differences were observed in hippocampal atrophy or tau levels.
- Cognitive decline is more pronounced in high-exposure participants, with greater dementia severity (CDR, $p = 0.002$) and faster cognitive decline (NTB, $p < 0.001$), while ADAS-Cog and MoCA scores remained unaffected.
- The detoxification gene EPHX1 is significantly associated with cognitive impairment ($p = 0.0356$), suggesting that exposure to environmental toxins, particularly PAHs, may contribute to neurodegeneration.

Results

Table 1. Sociodemographic Differences by Environmental Exposure Group

Variable	Overall (N=5101)	Low Exposure (N=4701)	Medium Exposure (N=133)	High Exposure (N=267)	p-value
Demographics					
Age (years), Mean ± SD	84.7 ± 10.4	85.4 ± 10.23	76.6 ± 8.56	75.7 ± 8.7	<0.001*
Gender, n (%)					
- Male	2561 (52.0%)	2456 (52.6%)	70 (52.6%)	120 (44.9%)	0.066
- Female	2466 (48.0%)	2245 (47.7%)	63 (47.3%)	147 (55.0%)	0.066
Ethnicity, n (%)					
- White	4813 (94.3%)	4433 (94.6%)	119 (90.15%)	242 (90.9%)	0.007*
- Black	255 (5.0%)	219 (4.7%)	13 (9.8%)	21 (7.9%)	0.007*
- Other	35 (0.7%)	32 (0.68%)	0 (0.0%)	3 (1.1%)	0.007*
Marital Status, n (%)					
- Married	3864 (73.3%)	3573 (73.6%)	92 (69.7%)	184 (69.7%)	0.107
- Widowed	618 (11.7%)	572 (11.8%)	19 (14.4%)	25 (9.5%)	0.107
-Divorced	519 (9.8%)	470 (9.7%)	15 (11.4%)	30 (11.4%)	0.107
-Never Married	236 (4.5%)	209 (4.3%)	6 (4.5%)	20 (7.6%)	0.107
-Unknown	25 (0.47%)	23 (0.47%)	0 (0.0%)	2 (0.76%)	0.107
-Domestic Partnership	10 (0.18%)	8 (0.16%)	0 (0.0%)	2 (0.76%)	0.107
Education Level, n (%)					
- Primary & Secondary	782 (15.3%)	554 (15.3%)	19 (9.9%)	33 (10.0%)	0.792
- Post-Secondary	997 (19.5%)	913 (25.3%)	22 (11.5%)	56 (16.9%)	0.792
- Graduate	3324 (65%)	3054 (59.4%)	88 (78.8%)	170 (72.9%)	0.792
Home Type, n (%)					
- House (owned or rented)	3601 (68.4%)	3387 (69.9%)	67 (50.8%)	133 (50.4%)	<0.001*
- Condo/Co-op (owned)	585 (11.11%)	549 (11.3%)	7 (5.3%)	26 (9.8%)	<0.001*
- Apartment (rented)	391 (7.42%)	355 (7.3%)	11 (8.3%)	22 (8.3%)	<0.001*
-Mobile Home	41 (0.77%)	41 (0.85%)	0 (0.0%)	0 (0.0%)	<0.001*
-Retirement Community	178 (3.38%)	164 (3.4%)	7 (5.3%)	6 (2.3%)	<0.001*
-Assisted Living	53 (1%)	48 (0.99%)	0 (0.0%)	4 (1.5%)	<0.001*
-Skilled Nursing Facility	8 (0.15%)	8 (0.16%)	0 (0.0%)	0 (0.0%)	<0.001*
- Other	54 (1%)	53 (1.1%)	0 (0.0%)	1 (0.38%)	<0.001*
Family History of AD, n(%)					
-No	2965 (66.9%)	2821 (66.8%)	39 (61.9%)	86 (67.7%)	0.684
-Yes	1459 (32.9%)	1391 (32.9%)	24 (38.1%)	41 (32.3%)	0.684
Co-Morbidity, n(%)					
-No	19 (0.35%)	18 (0.37%)	0 (0.0%)	1 (0.37%)	0.615
-Yes	5280 (99.6%)	4859 (99.6%)	133 (100%)	266 (99.6%)	0.615
Serious Adverse Event, n(%)					
-No	4905 (92.8%)	4528 (93.0%)	123 (92.5%)	243 (91.0%)	0.454
-Yes	376 (7.11%)	340 (6.9%)	10 (7.5%)	24 (8.9%)	0.454

Note: This table highlights significant differences in age, ethnicity, and home type across environmental exposure groups, while education, co-morbidities, and adverse events showed no significant variation.

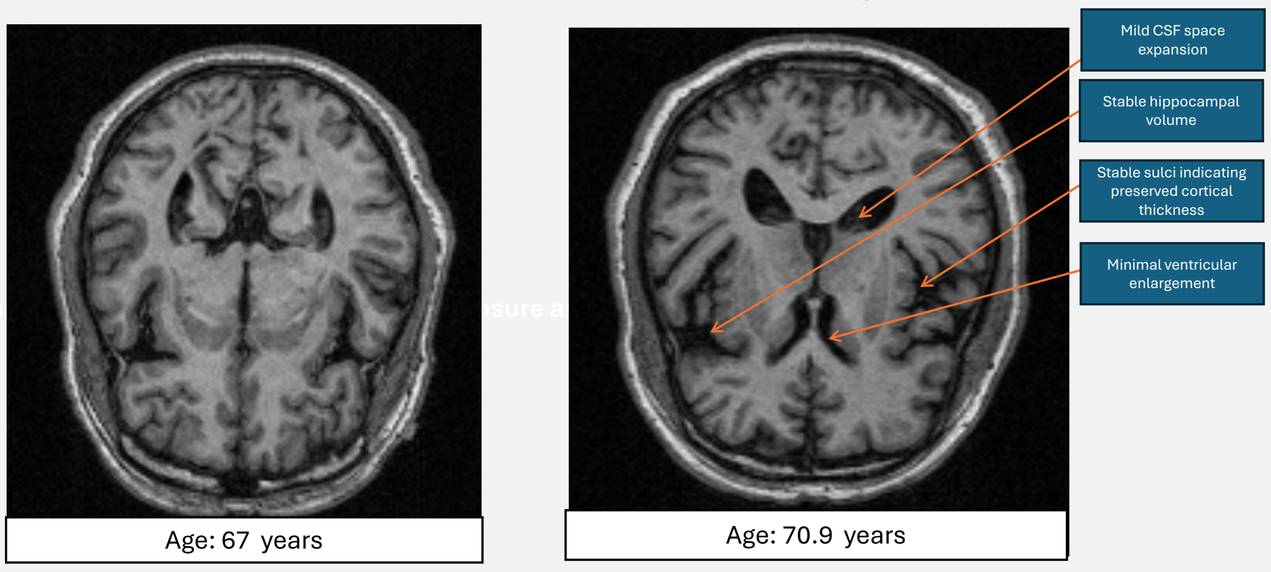
Alzheimer's cases are expected to triple by 2050, yet environmental risk remains overlooked. Our findings show that high environmental exposure is linked to 46% lower CSF Amyloid-β ($p < 0.001$)—a key indicator of increased amyloid plaque buildup and faster disease progression.

Table 2. Cognitive Assessments by Environmental Exposure Group

Variable	Overall (N=5101)	Low Exposure (N=4701)	Medium Exposure (N=133)	High Exposure (N=267)	p-value
Baseline Cognitive Function					
ADI Score	3.8 ± 2.53	4.0 ± 4.24	3.9 ± 2.43	3.77 ± 2.57	0.886
MMSE (Mini-Mental State Exam), Mean ± SD	26.01 ± 4.37	25.9 ± 4.40	26.9 ± 3.11	26.42 ± 3.91	0.011*
ADAS-Cog, n(%)					
-Fold a letter	738 (55.19%)	717 (55.0%)	2 (50%)	5 (55.5%)	0.711
-Put letter in envelope	339 (25.35%)	330 (25.4%)	1 (25%)	1 (11.1%)	0.711
-Seal envelope	147 (10.99%)	145 (11.1%)	0 (0.0%)	2 (22.2%)	0.711
-Address envelope	65 (4.86%)	64 (4.9%)	1 (25%)	0 (0%)	0.711
-Indicate where stamp goes	27 (2.02%)	26 (1.9%)	0 (0.0%)	1 (11.1%)	0.711
-No completed	5 (0.37%)	5 (0.38%)	0 (0.0%)	0 (0.0%)	0.711
Cognitive Decline (EDCog)	19.66 ± 10.3	20.46 ± 12.43	19.33 ± 7.29	19.06 ± 9.29	0.354
MoCA (Montreal Cognitive Assessment)	12.95 ± 4.97	12.86 ± 5.01	13.28 ± 4.96	13.46 ± 4.7	0.260
Clinical Dementia Rating (CDR)	1.82 ± 2.54	1.82 ± 2.53	2.51 ± 3.12	2.06 ± 2.86	0.002*
Cognitive Decline (NTB)	4.28 ± 1.09	4.29 ± 1.08	3.9 ± 1.4	3.85 ± 1.29	<0.001*
Baseline Cognitive Decline	20.2 ± 9.7	21.2 ± 10.29	10.2 ± 4.6	13.2 ± 6.07	<0.001*

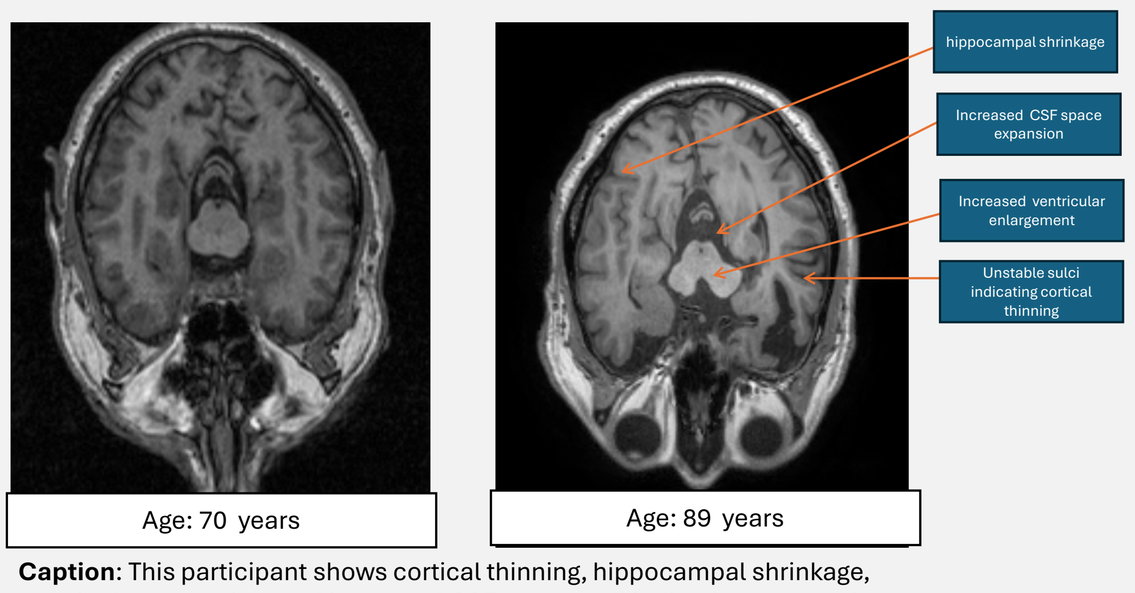
Note: This table compares cognitive function across low, medium, and high environmental exposure groups. Significant differences were found in MMSE ($p = 0.011$), CDR ($p = 0.002$), NTB ($p < 0.001$), and baseline cognitive decline ($p < 0.001$), while ADAS-Cog and MoCA showed no significant variation.

Case 022_S_0004: Low Environmental Exposure and Cognitive Function



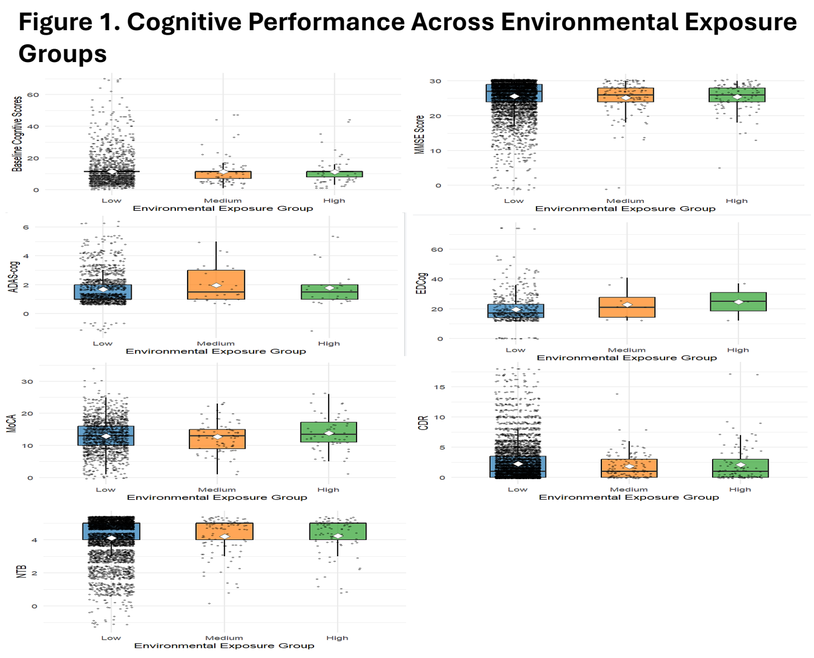
Caption: This participant had low environmental exposure with stable cognitive function and no significant neurodegeneration.

Case 123_S_0072: High Environmental Exposure and Cognitive Function



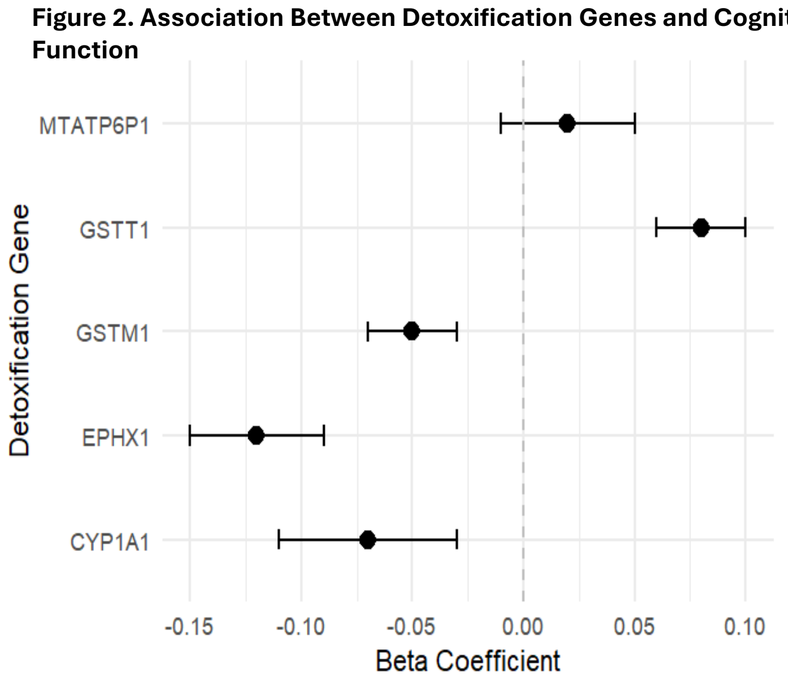
Caption: This participant shows cortical thinning, hippocampal shrinkage, ventricular expansion, and increased CSF spaces, all indicating progressive brain atrophy associated with Alzheimer's disease.

Figure 1. Cognitive Performance Across Environmental Exposure Groups



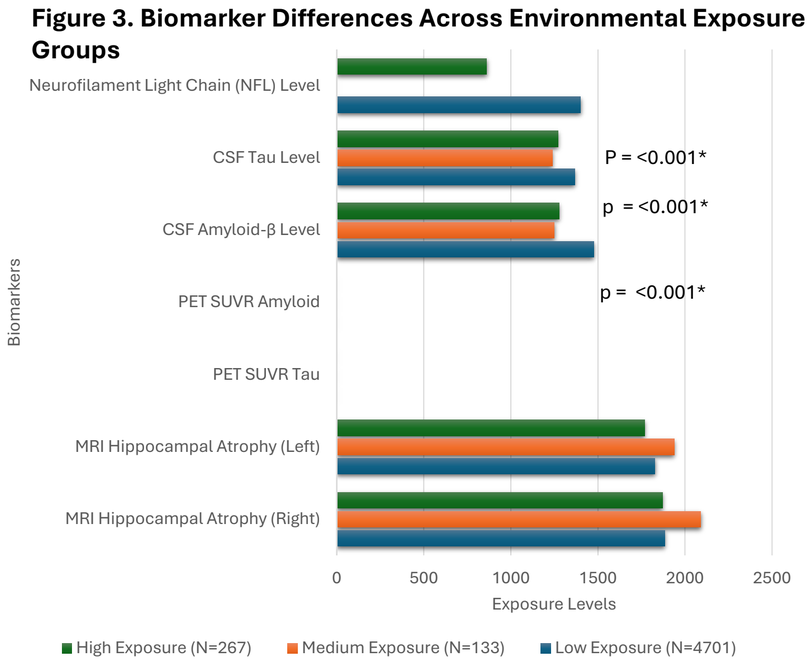
Caption: Cognitive scores vary by environmental exposure, with significant differences observed in MMSE, CDR, NTB, and baseline cognitive decline, while ADAS-Cog and MoCA show no significant variation.

Figure 2. Association Between Detoxification Genes and Cognitive Function



Caption: EPHX1 and CYP1A1 show the strongest negative associations with cognitive function, suggesting a potential link between detoxification gene activity and neurodegeneration in individuals with higher environmental exposure.

Figure 3. Biomarker Differences Across Environmental Exposure Groups



Caption: Higher environmental exposure is associated with lower CSF Amyloid-β levels and higher PET SUVR Amyloid, while MRI hippocampal atrophy and CSF Tau levels show no significant variation across exposure groups.

Acknowledgement

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