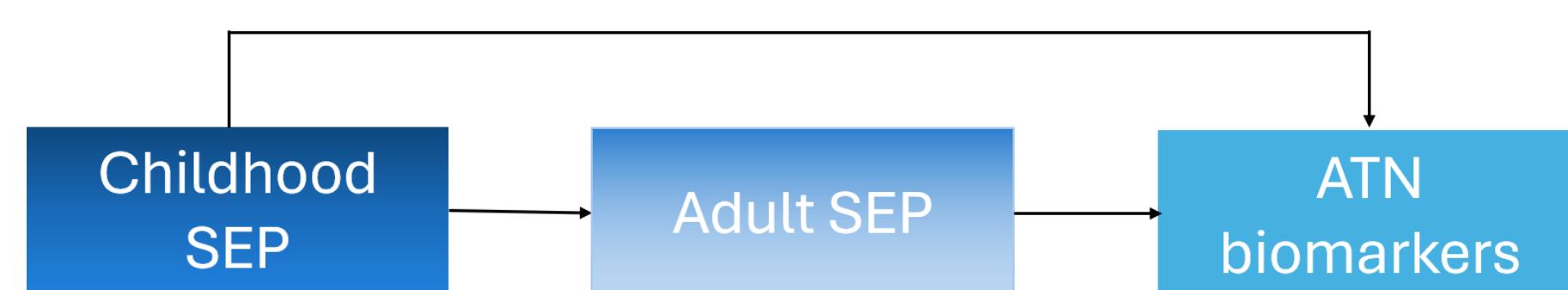


Introduction

- Low socioeconomic position (SEP) over the life-course has been associated with lower cognitive function, greater cognitive decline, and smaller MRI brain volumes in later life
- However, its association with pathological markers of Alzheimer's Disease (AD) and AD-Related Dementias (AD/ADRD), including plasma Amyloid[A], Tau[T], and Neurodegeneration[N] [ATN] biomarkers, is not well understood
- As plasma ATN biomarkers may play a key role in detecting the preclinical phase of AD, identifying drivers across life-course stages is pivotal to determining targets for earlier interventions

Objective

- To assess the association between childhood and adult SEP with plasma ATN biomarkers among middle-aged and older Hispanic/Latino adults
- **Hypotheses:** We hypothesized that lower childhood and/or adult SEP would be associated with lower Amyloid but higher p-Tau and neurodegeneration biomarkers



Methods

Study: We used data from the Hispanic Community Health Study/Study of Latino (HCHS/SOL) and Investigations of Neurocognitive Aging (SOL-INCA) ancillary study. HCHS/SOL is a community-based cohort study conducted in four major U.S urban areas (Chicago, IL; Bronx, NY; Miami, FL; San Diego, CA)

Population: 6270 adults 45 and older who participated in HCHS/SOL visit 1 (2008-2011) and SOL-INCA (2015-2018)

Life-course SEP:

- **Childhood SEP:** We used participants' reports of the highest education achieved by either the father or mother, and classified it as high school or above (reference), and less than high school, as a proxy for childhood SEP
- **Adult SEP:** We built an index combining participants' self-reported educational attainment, current occupation, annual household income, and house ownership at visit 1 (score 0 to 8) and classified as high SEP (score 3-8, reference) and low SEP (score <3)

Plasma ATN biomarkers:

Biomarkers of AD pathology: Amyloid β 42 (A β 42), phosphorylated-Tau (p-Tau181), A β 42/A β 40, p-Tau181/ A β 42

Non-specific AD pathology biomarkers: neurofilament light chain (NfL) and fibrillary acidic protein (GFAP)

- Measured on plasma samples collected at visits 1 and 2 in picograms per milliliter (pg/mL)
- Assays were performed on the Quanterix HD-X Analyzer using ultra-

sensitive single molecule array (SIMOA) kits (Quanterix, Billerica, MA)

- Values above or below the detection threshold and extreme outliers (10 SD above the mean) were excluded from the statistical analysis

Covariates: Demographic: year of birth with splines at 1949, 1959, and 1969, sex, place of birth, Hispanic/Latino background, marital status, health insurance, field center; behavioral: smoking status, alcohol use, physical activity; health: BMI, hypertension, diabetes, prevalent CVD or stroke, GFR, and ApoE-4 selected for each life-course SEP exposure

Analysis:

- Given the life-course approach with time-varying exposures and confounders we:
 - fitted weighted linear regression models using inverse probability weighting and marginal structural models
 - accounted for the complex sampling design
 - obtained the controlled direct effect (CDE, and 95% CI) of each life-course SEP exposure on each plasma ATN biomarker at visit 1 and visit 2
- Elapsed time between visits for biomarkers at visit 2
- Multiple imputation due to missing data on parental education, household income, and covariates
- Effect modification by age, sex, place of birth, and ApoE-4

Results

Table 1. Socio-demographic characteristics of the study population at visit 1 by sex

Characteristic	Overall (n=6270)	Males (n=2239)	Females (n=4031)
Weighted % or mean (SD)			
Age (years), mean (SD)	56.4 (8.0)	56.0 (7.0)	56.7 (8.9)
Center, No. (%)			
Bronx	1398 (27.3)	28.5	25.8
Chicago	1557 (12.5)	11.7	13.5
Miami	1688 (36.4)	36.1	37.8
San Diego	1623 (23.8)	24.6	22.8
Place of birth, No. (%)			
Born in the 50 US. States/DC	554 (8.3)	9.3	7.5
Born outside the 50 US. States/DC	5708 (91.6)	90.7	92.5
Childhood SEP: parental education, No. (%)			
Low: <HS	3849 (64.4)	62.5	66.1
High: HS+	1732 (35.5)	37.5	33.9
Adult SEP, No. (%)			
Low	2295 (39.7)	37.8	41.5
High	3433 (60.2)	62.1	58.4

SD: Standard Deviation; SEP: Socioeconomic position; HS: High school. Adult SEP: High (score ≥ 3), low (score <3)

Table 2. Behavioral and characteristics of the study population at visit 1 by sex

Characteristic	Overall (n=6270)	Males (n=2239)	Females (n=4031)
Weighted % or mean (SD)			
Current smoker (Yes), No. (%)	1094 (18.5)	22.5	15.0
Alcohol use disorder, No. (%)			
No current use	3558 (54.3)	41.9	64.8
Low-risk drinker	2467 (41.9)	51.4	33.9
At-risk drinker	235 (3.8)	6.7	1.4
Physical activity, No. (%)			
Inactive or low activity	3555 (65.0)	53.3	74.9
Medium activity	1018 (19.8)	23.8	16.6
High activity	729 (15.1)	22.9	8.5
BMI, mean (SD)	29.7 (5.4)	28.9 (4.3)	30.4 (6.2)
GFR, mean (SD)	85.4 (20.2)	85.5 (18.1)	85.3 (21.8)
Hypertension (Yes), No. (%)	2742 (47.0)	54.9	48.6
Diabetes (Yes), No. (%)	1737 (28.7)	28.1	29.2
ApoE-4 carrier, No. (%)	1366 (22.4)	22.4	22.3

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Figure 1. Association between childhood and adult SEP and plasma ATN biomarkers at visit 1 in the overall population and by sex

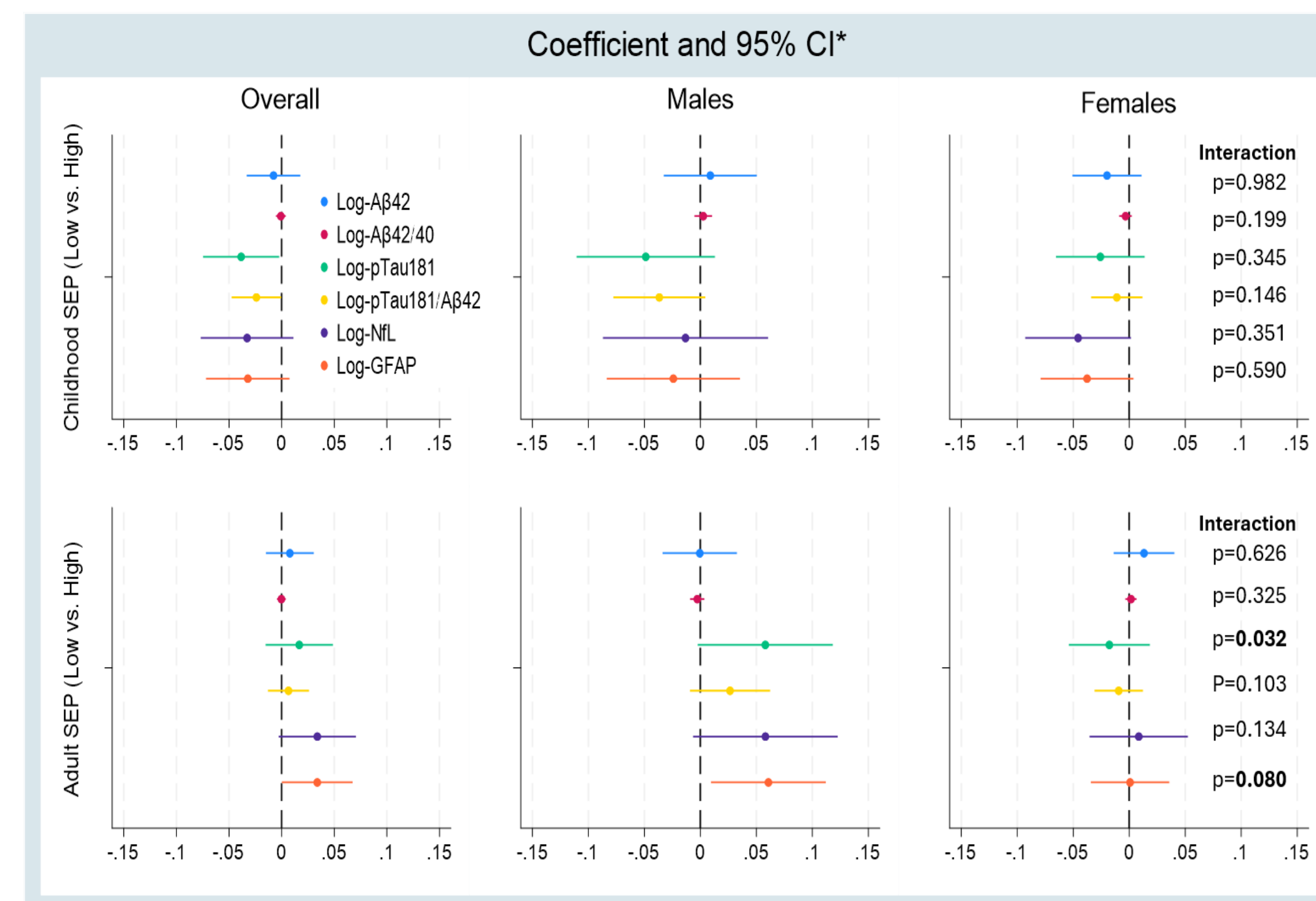
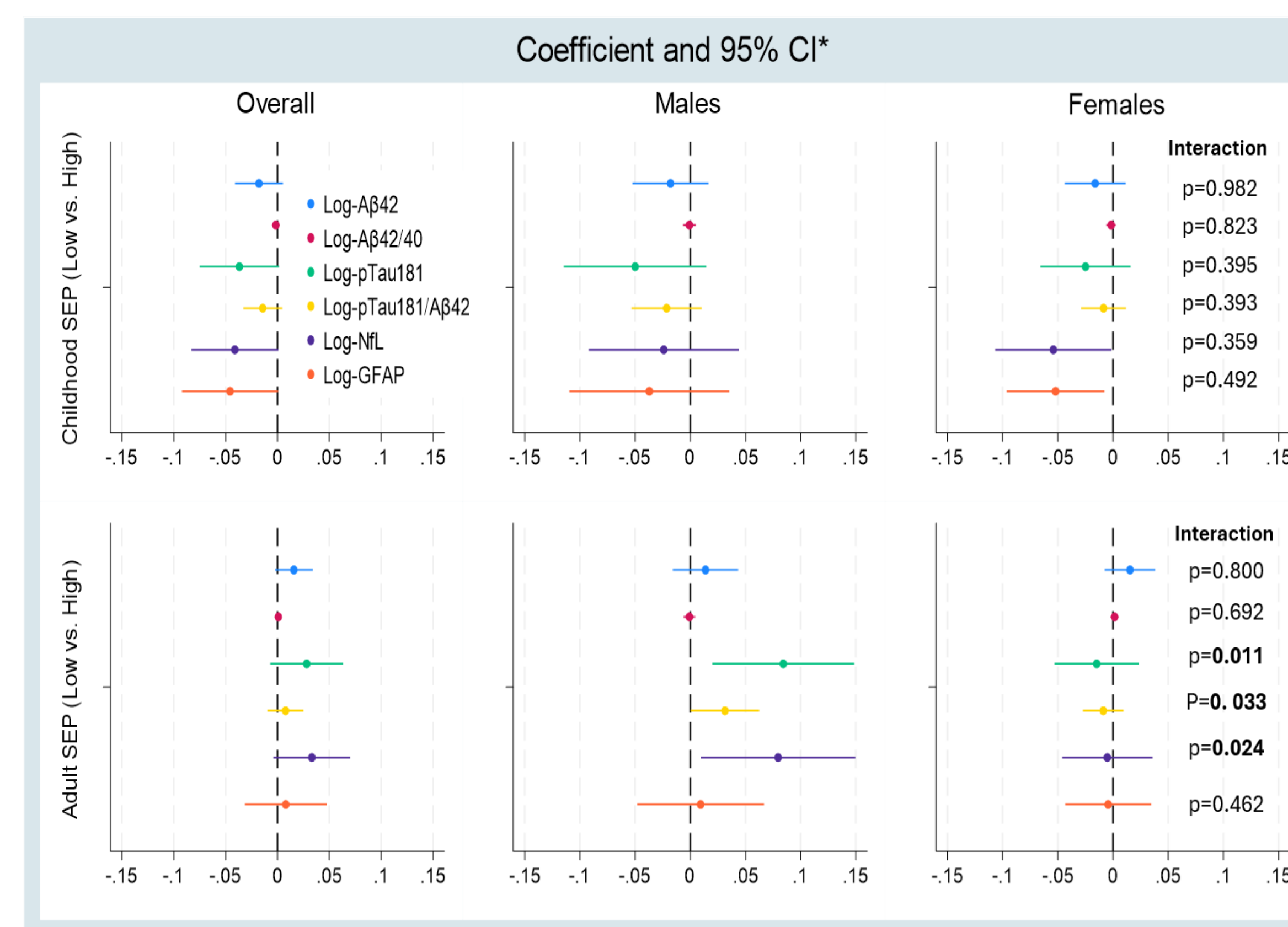


Figure 2. Association between childhood and adult SEP and plasma ATN biomarkers at visit 2 in the overall population and by sex



Footnote for Figures 1, 2: *Weighted linear regression models accounted for complex sampling design and covariates using inverse probability weighting

Conclusions

- Childhood SEP was not associated with ATN biomarkers in the overall population. However, paradoxical associations were found for p-Tau181 (Fig 1), NfL, and GFAP (Fig 2), particularly among females
- Adult SEP was not associated with ATN biomarkers. However, among males, lower adult SEP was associated with higher p-Tau181, p-Tau181/A β 42, GFAP, and NfL
- We did not find evidence of effect modification by age, place of birth, and ApoE-4
- These findings suggest more AD pathology (p-Tau) and neurodegeneration (NfL and GFAP) among Hispanic/Latino males facing disadvantageous SEP in adulthood. Conversely, potential survival bias may explain the paradoxical associations observed with childhood SEP in females