

Elevated plasma neurofilament light chain is associated with higher left-right asymmetry of gait measures in cognitively normal adults

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INTRODUCTION

- Gait analysis has potential to be a screening tool for identifying older adults at risk of developing mild cognitive impairment and Alzheimer's disease (AD).
- While prior work primarily focused on gait velocity, recent studies have supported a more multidimensional approach.
- In this study, we aimed to assess the left-to-right asymmetry index (AI) of quantitative gait measures and their associations with plasma AD biomarkers in cognitively normal older adults.

HYPOTHESIS

Different plasma AD biomarkers will have unique correlations to asymmetry indices of gait variables in normal/preclinical older adults

METHODS

- We conducted a cross-sectional study of 106 cognitively normal older adults from the NYU Alzheimer's Disease Research Center (see Figure 1) who were cognitively unimpaired by consensus diagnosis and completed quantitative gait assessment using the GAITRite electronic walkway.
- Participants performed eight walkway passes at a single study visit, and asymmetry indices were calculated for step length, toe-in/toe-out angle, foot width, and leg length.
- Plasma A β 42, A β 40, total tau, NfL, and pTau181 were measured using Quanterix SIMOA, and their log-transformed associations with gait asymmetry were examined using multivariable linear regression models.

Figure 1: Cohort characteristics

Cohort Characteristics	N=106
Age (years)	73.5 +/- 6.8
Female (%)	72 (67.9%)
ApoE4 Carrier (%)	42 (39.6%)
Mean Years of Education	17 years
Race	
White (%)	67 (63.2%)
Black/African American (%)	36 (34%)
Asian (%)	2 (1.8%)
American Indian or Alaskan (%)	1 (0.94%)
Average Step Length (cm)	
Left	61.66
Right	61.60
Average Foot Width (cm)	
Left	8.70
Right	8.74
Average Leg Length (cm)	
Left	96.39
Right	96.20
Average Toe-in and/or Toe-out (degree)	
Left	5.17
Right	7.74

Figure 2. Relationship between AI in Step length and plasma levels of Neurofilament-light (NfL)

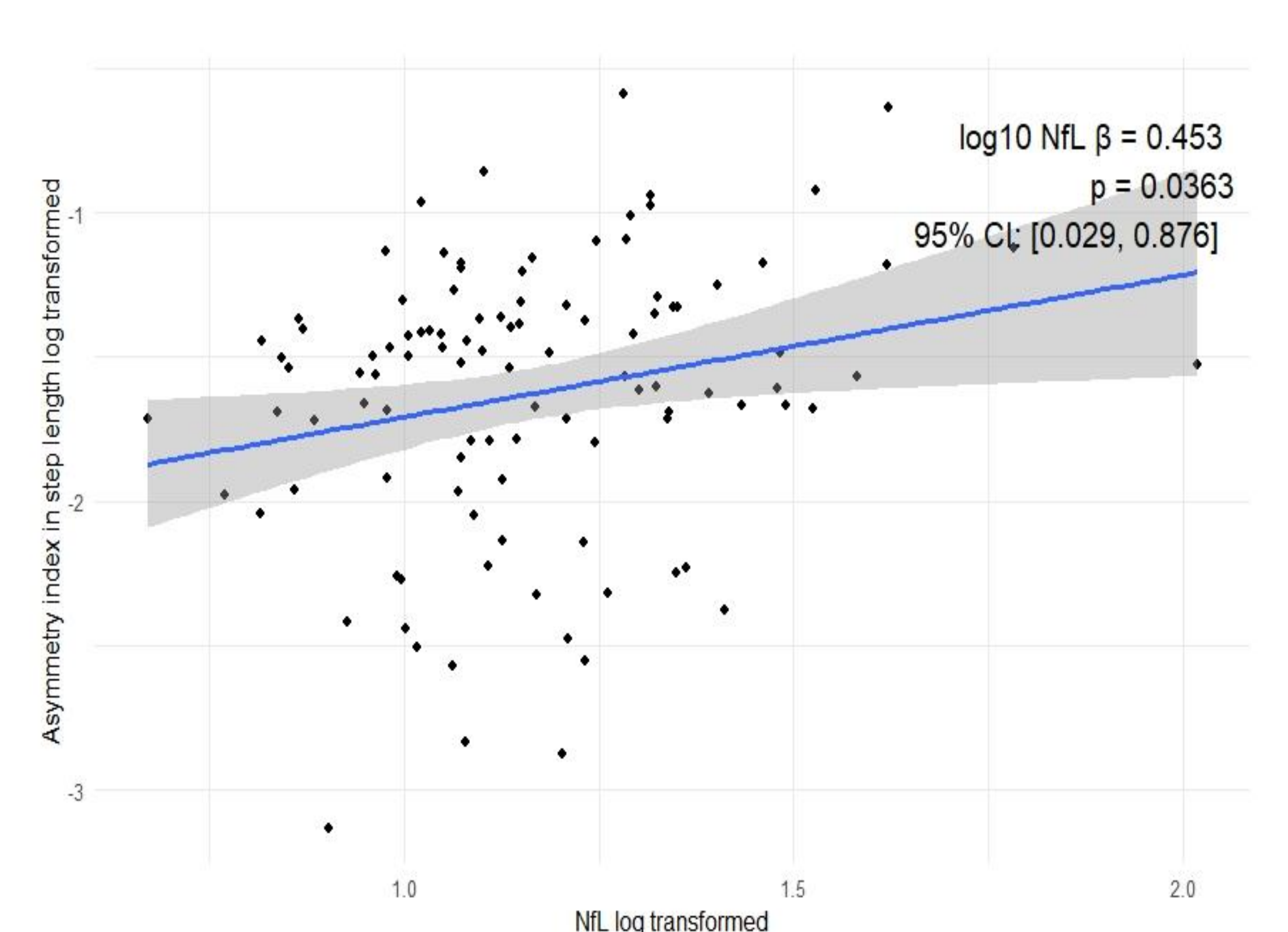


Figure 2. Scatter plot showing the association between log10 transformed NfL and AI in step length after adjusting for sex and APOE4 status. The solid line represents the fitted linear regression line, and the shaded area indicates the 95% confidence interval.

RESULTS

- We examined the association between log transformed NfL and AI in step length adjusting for sex and APOE4 status.
- Scatter plot in **Figure 2.** shows each 1% increase in plasma NfL was associated with a 0.45% increase in step length asymmetry ($\beta = 0.453$, 95% CI: 0.03 to 0.87; $p = 0.036^*$).
- Sex and APOE4 were not significant predictors in the adjusted model (sex: $\beta = -0.085$, SE = 0.098, $p = 0.389$; APOE4: $\beta = -0.086$, SE = 0.096, $p = 0.373$).
- AI of other gait measures did not show significant associations with any plasma markers.

CONCLUSIONS

Asymmetry of step length uniquely correlates with plasma NfL in cognitively unimpaired older adults, thus suggesting that this may relate to preclinical cerebral axonal injury. This supports future work on the relationship of step length symmetry to neurodegeneration and longitudinal outcomes on the AD spectrum.

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