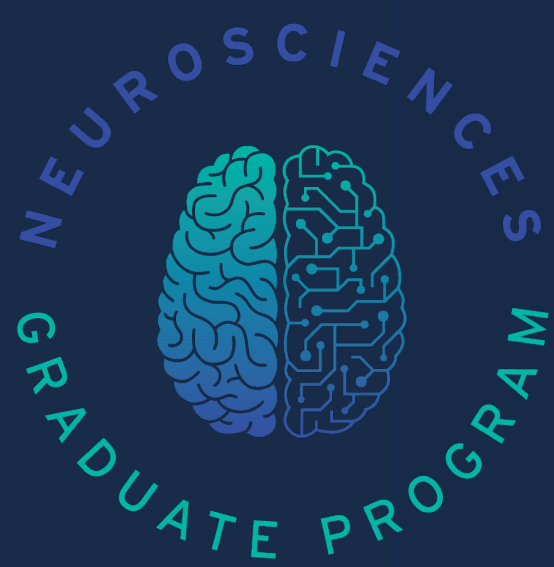


Moderate activity in the morning and evening differentially relates to longitudinal changes in amyloid-β and tau pathology

#1121

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INTRODUCTION

Background: Physical activity is a promising lifestyle intervention for Alzheimer’s disease, but whether **physical activity timing** impacts pathology remains unclear.

Purpose: This longitudinal study examined whether time-segmented moderate activity was differentially related to amyloid-β and tau pathology and explored potential vascular, neurotrophic, and inflammatory pathways.

METHODS

Sample: 53 sedentary older adults ages 55-79 with **objective early cognitive impairment** in a 6-month randomized trial of moderate-intensity walking

Assessments: Actigraphy (~3-4 weeks), amyloid and tau PET, phase-contrast MRI, and blood biomarker assays at baseline and 6 months

Predictors: Moderate activity (minutes) in the **morning** (8AM-12PM), **afternoon** (12PM-4PM), **evening** (4PM-8PM), and **daily total**

Outcomes: PET standardized uptake value ratio (SUVR) for amyloid-β composite and tau Braak ROIs I/II, III/IV, and V/VI

Exploratory variables:

- Cerebral blood flow (N = 50):** arterial pulsatility (arterial stiffness), systolic peak (peak flow rate), stroke volume (blood volume displacement)
- Blood biomarkers (N = 36):** brain-derived neurotrophic factor (BDNF) and tumor necrosis factor-alpha (TNF-α)

Statistics: Linear regression analyses examined change-change associations between moderate activity and amyloid-β/tau burden, BDNF, and TNF-α, adjusting for intervention arm, age, sex, *APOE4*, BMI, and baseline outcome. Moderation analyses tested cerebral blood flow as a modifier of associations between moderate activity and amyloid-β/tau burden.

RESULTS

Table 1. Participant characteristics

Characteristic	N = 53
Age at baseline (mean, SD)	66.77 (6.37)
Women (%)	56.60
Body mass index in kg/m ² (mean, SD)	26.61 (4.31)
APOE4 carrier status (%)	24.53
Ethnicity, Hispanic/Latino (%)	7.55
Race (%)	
White	83.02
African American	9.43
Asian	3.77
Other	1.89
More than one race	1.89

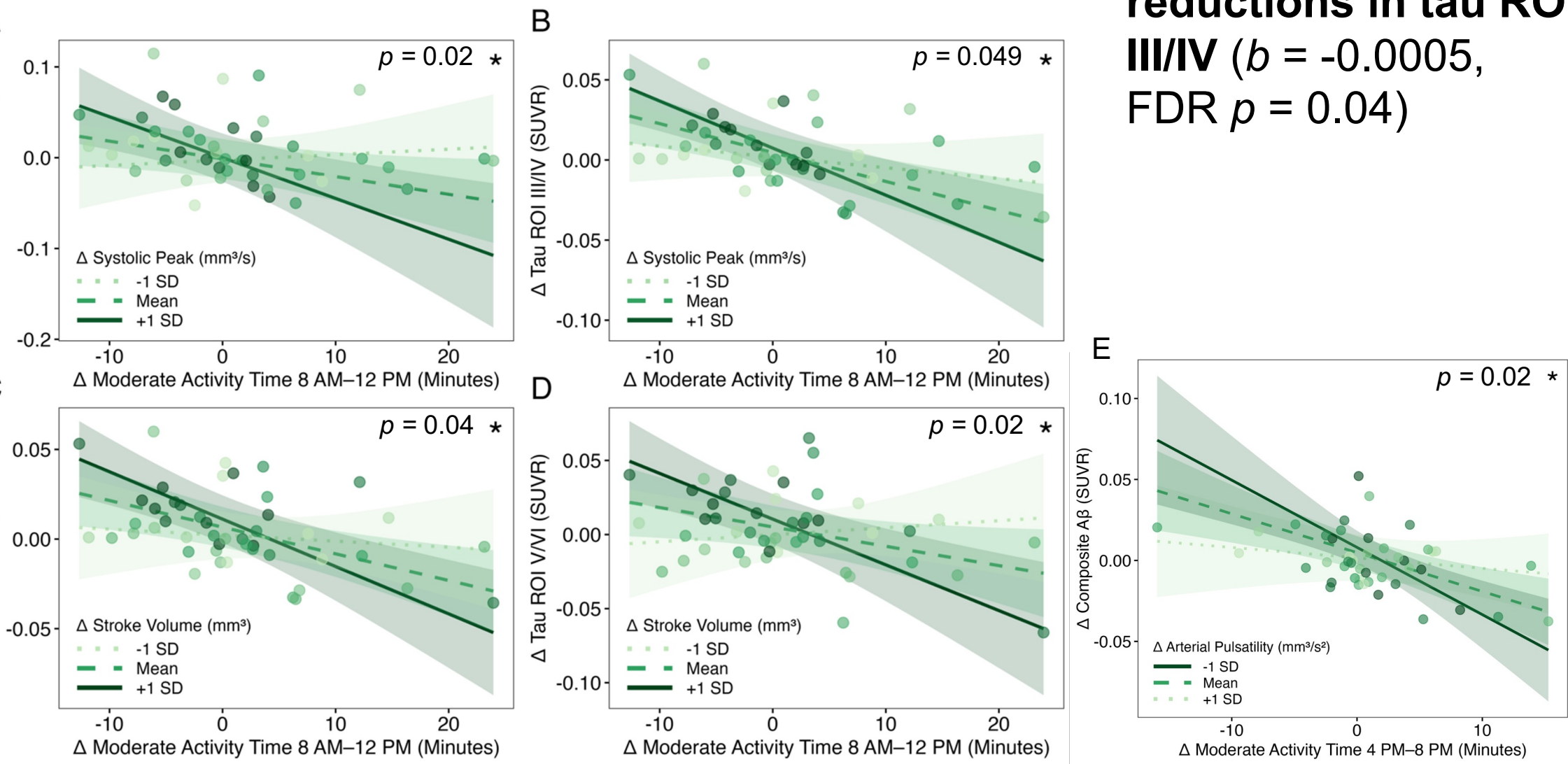


Figure 2. Systolic peak (A-B) and stroke volume (C-D) modified the morning moderate activity–tau associations, while arterial pulsatility (E) modified the evening moderate activity–amyloid-β association

Figure 1. Increases in evening moderate activity were associated with reductions in amyloid-β (A), while increases in morning moderate activity were associated with reductions in tau ROIs I/II (B), III/IV (C), and V/VI (D)

Increases in daily moderate activity were only associated with reductions in tau ROIs III/IV ($b = -0.0005$, FDR $p = 0.04$)

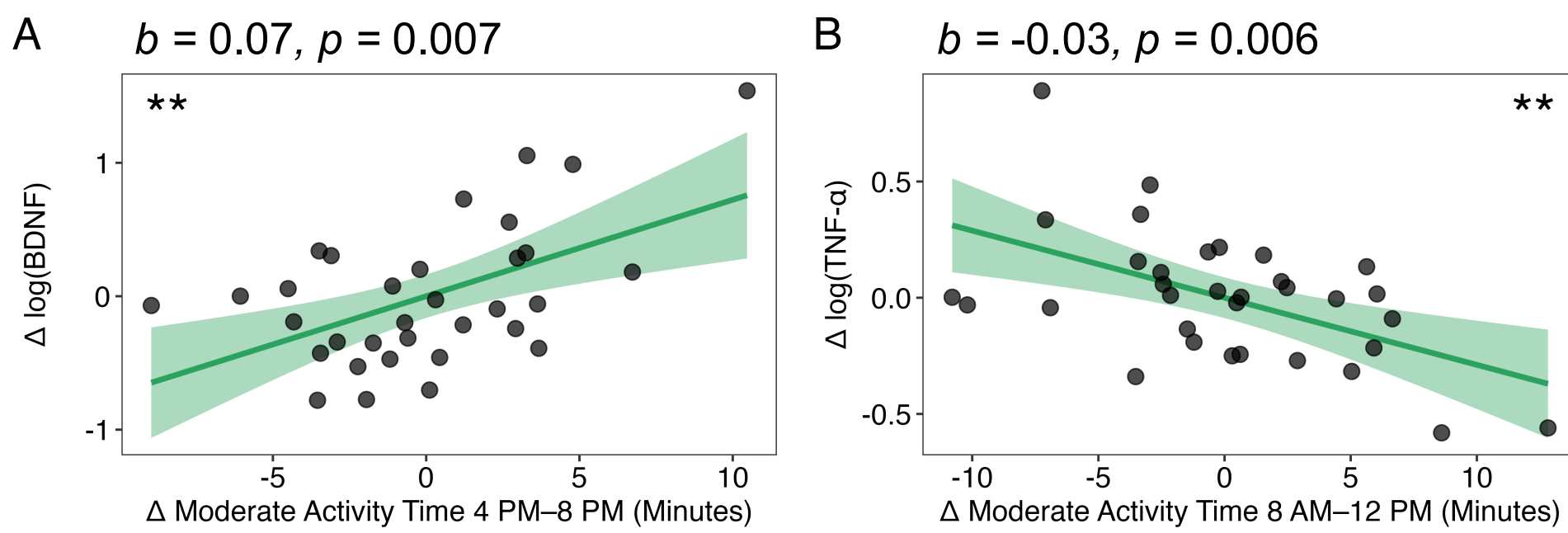
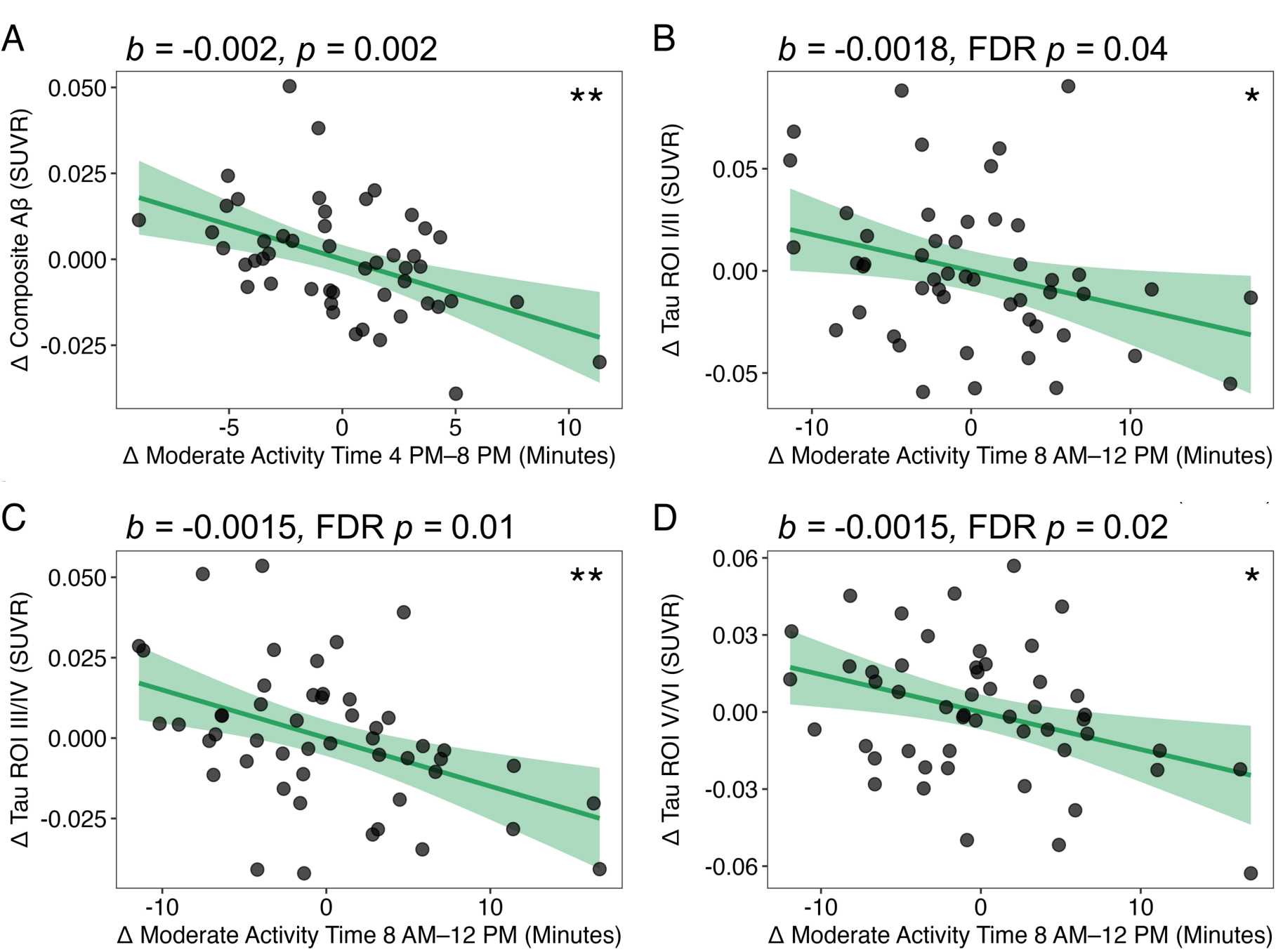


Figure 3. Increases in evening moderate activity were associated with increases in BDNF (A), while increases in morning moderate activity were associated with reductions in TNF-α (B)

Neither biomarker was associated with daily moderate activity

CONCLUSIONS

Timing of physical activity may differentially impact Alzheimer’s disease pathology, with morning moderate activity linked to tau reductions and evening moderate activity linked to amyloid-β reductions. Vascular, neurotrophic, and inflammatory pathways may contribute to these timing-specific associations.

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