

Physical Activity and Sleep Quality on Preclinical Neurodegeneration in Older Adults at Risk for Alzheimer's Disease

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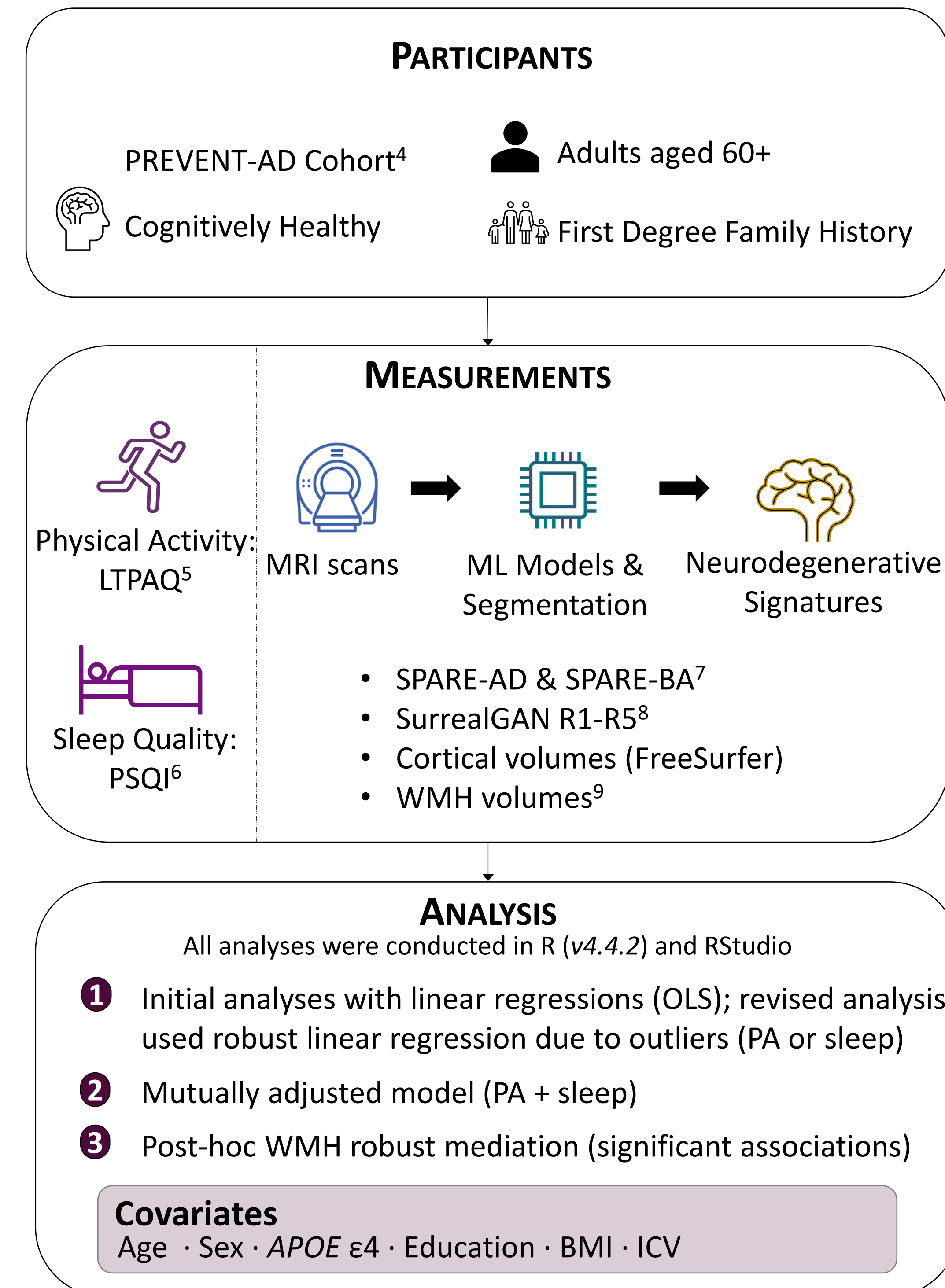
BACKGROUND AND OBJECTIVES

- Alzheimer's disease (AD) is an age-associated neurodegenerative disorder, with modifiable risk factors offering actionable intervention points¹.
- Low physical activity (PA) and poor sleep contribute to AD-related neurodegeneration; however, their independent contributions in preclinical stages remains underexplored².
- White matter hyperintensities (WMH), a cerebrovascular marker, may mediate these relationships but have not been formally tested as a mediator³.
- We examined the independent associations of PA and sleep quality with neurodegeneration in preclinical AD and evaluated WMH as a potential mediator.

METHODS

STUDY DESIGN AND PARTICIPANTS

- Cross-sectional secondary data analysis investigating the associations of PA and sleep in cognitively healthy older adults with a first-degree family history of AD.



- Previous analysis from OLS regressions showed significant associations for PA (lingual gyrus, pericalcarine and SurrealGAN-R3) and sleep (rostral anterior cingulate and SurrealGAN-R1). Current results reflect updated robust linear regression approach¹⁰.

Table 1. Baseline Demographic and Clinical Information

Variables	Overall (n = 137)
Age, mean (SD)	65.69 (5.18)
Female, n (%)	102 (74.5)
Educational years, mean (SD)	15.20 (3.16)
Body Mass Index, kg/m ² , mean (SD)	26.59 (4.54)
APOE ε4 Carrier, n (%)	51 (37.2)
Intracranial Volume, cm ³ , mean (SD)	1531.74 (135.24)
Sleep Quality (PSQI), mean (SD)	4.88 (2.99)
PA, MET-hr/week, median [IQR]	30.09 [14.08, 46.85]
SPARE-AD, mean (SD)	-0.98 (0.51)
SPARE-BA, mean (SD)	66.05 (8.90)
WMH Volume, cm ³ (median [IQR])	1.37 [0.76, 3.26]

Note: APOE ε4 = apolipoprotein E ε4; PSQI = Pittsburgh Sleep Quality Index; PA = physical activity; MET = metabolic equivalent of task; SPARE-AD = Spatial Patterns of Atrophy for Recognition of Alzheimer's Disease; SPARE-BA = Spatial Patterns for Recognition of Brain Ageing; WMH = white matter hyperintensities. WMH volumes available for n = 83 (39.4% missing).

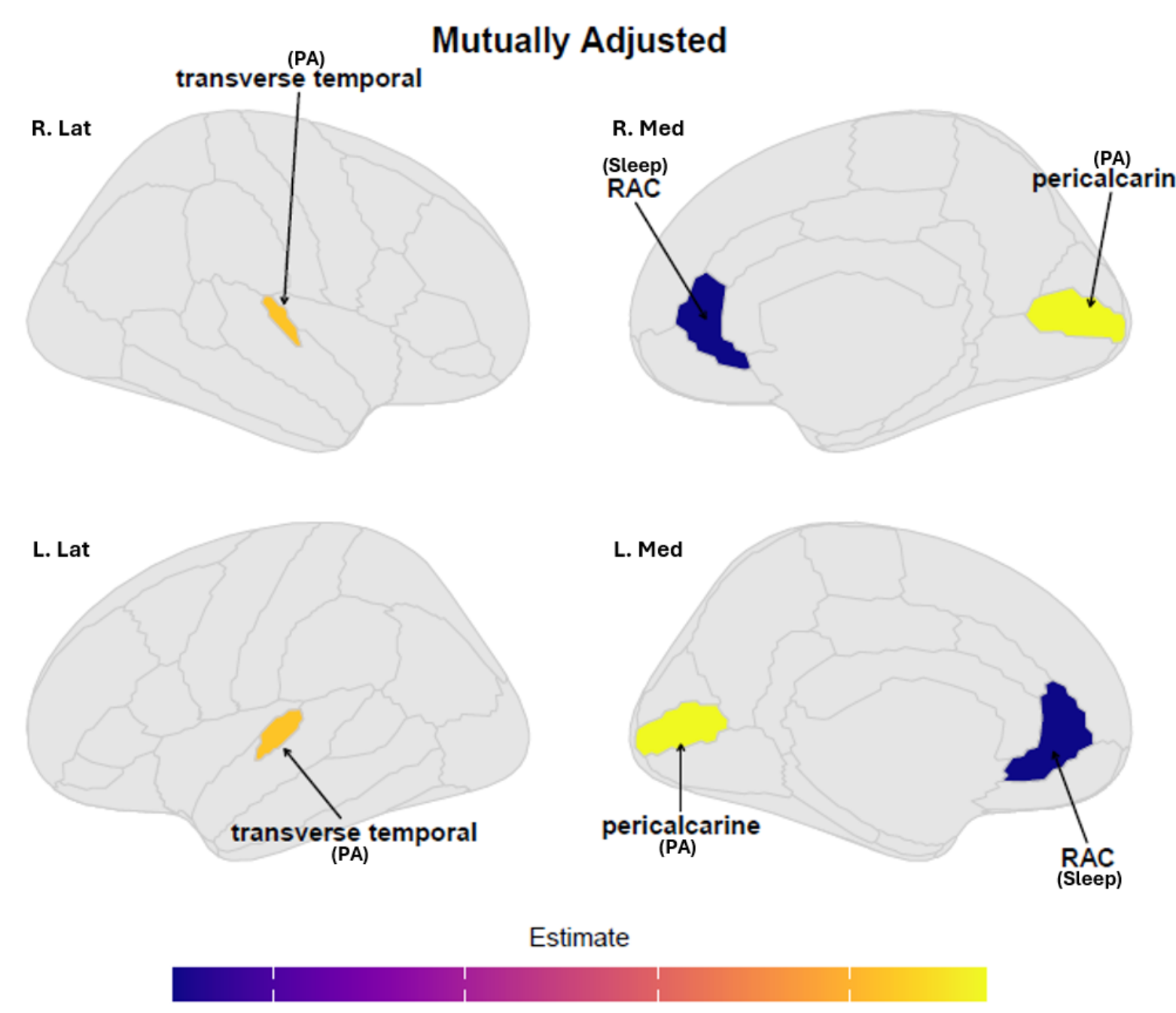


Figure 2. Mutually adjusted associations with regional cortical volume. All labeled regions survived mutual adjustment for both PA and sleep quality (unadjusted p < 0.05). Transverse temporal and pericalcarine: PA. Rostral anterior cingulate (RAC): sleep quality.

DISCUSSION AND CONCLUSIONS

- In robust linear regression models, PA showed complex, region-dependent associations with neurodegeneration, possibly reflecting subclinical atrophy already present in this familial risk population.
- PA may selectively protect regional grey matter volumes, independent of sleep quality.
- Poor sleep quality independently predicted greater neurodegeneration across data-driven and regional outcomes, independent of PA.
- WMH did not mediate these associations in this preliminary analysis; whether vascular pathways become more prominent at different disease stages remains an open question for future work.
- Findings are exploratory and should be interpreted with caution given the risk of Type I error due to multiple comparisons.

RESULTS

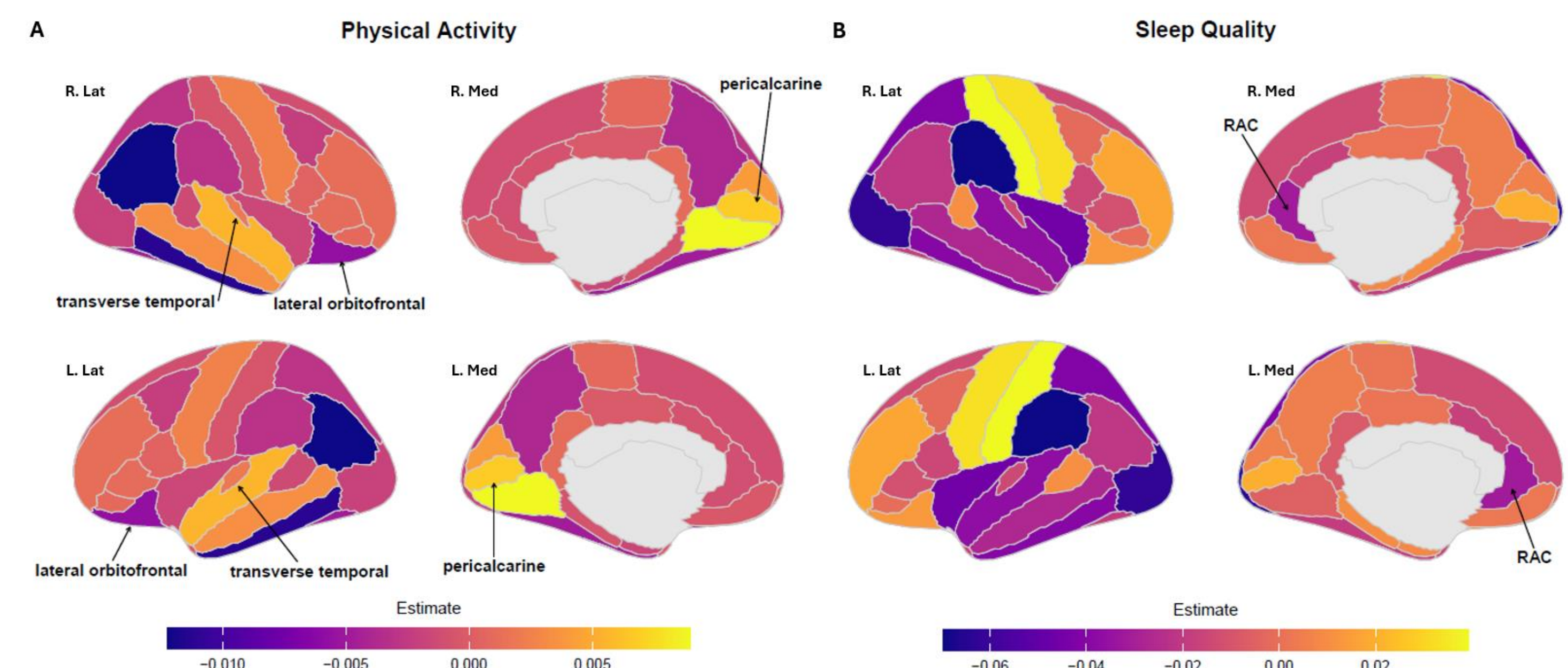


Figure 1. Regional cortical volume associations with physical activity (A) and sleep quality (B). Warm/yellow tones indicate positive associations; cool/blue tones indicate negative associations. Note: higher PSQI = worse sleep quality. Labeled regions reached statistical significance (unadjusted p < 0.05), except RAC (unadjusted p = 0.051). RAC = rostral anterior cingulate.

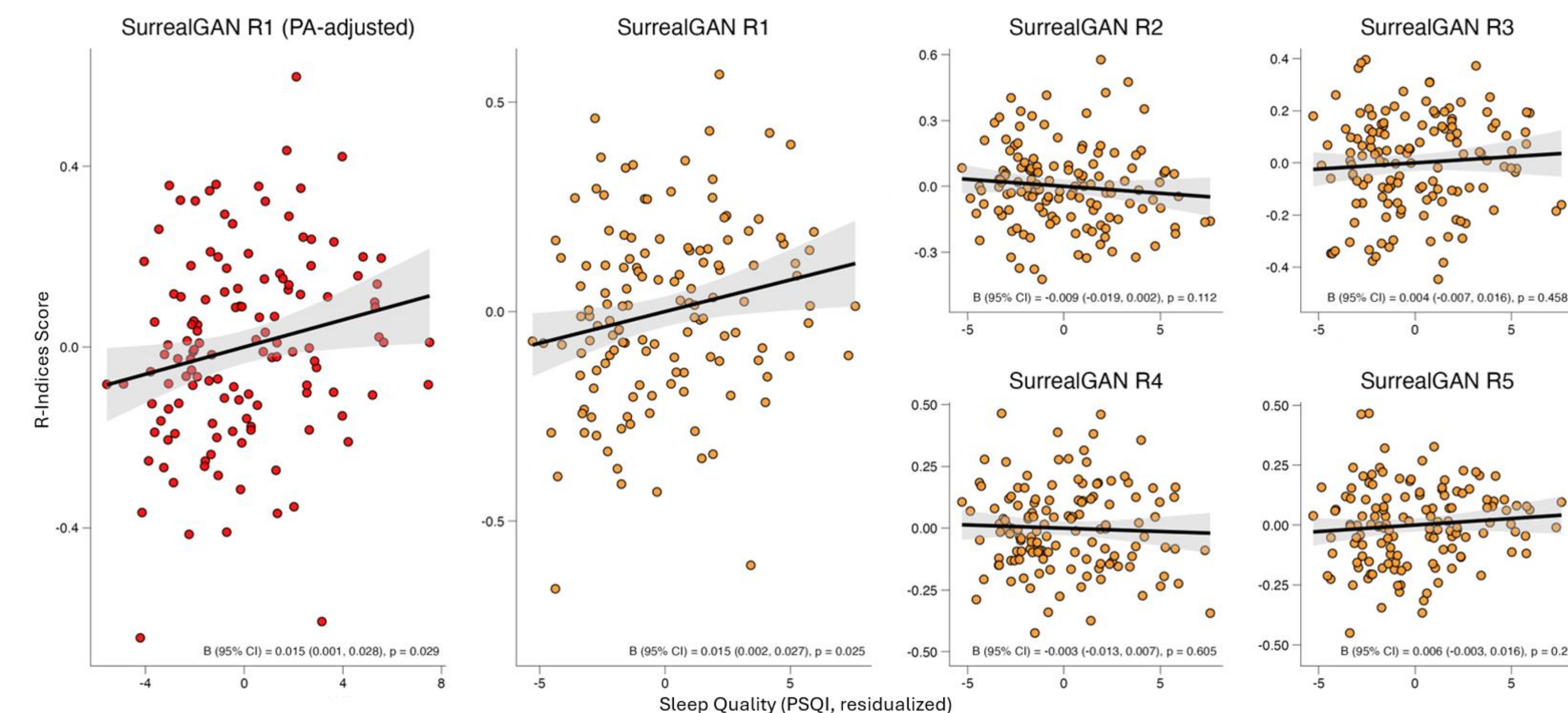


Figure 3. Associations between covariate-adjusted residuals of sleep quality and SurrealGAN-indices (R1-R5); R1 is shown with (red) and without (orange) additional physical activity adjustment.

This represents a preliminary analysis; a more comprehensive investigation including moderation by sex, APOE ε4 status, and AD biomarker positivity is ongoing.

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Acknowledgments

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