

Independent Associations of Sleep Fragmentation and Respiratory Disturbances with Plasma Alzheimer’s Disease - Related Pathologies: A Cross-Sectional Study

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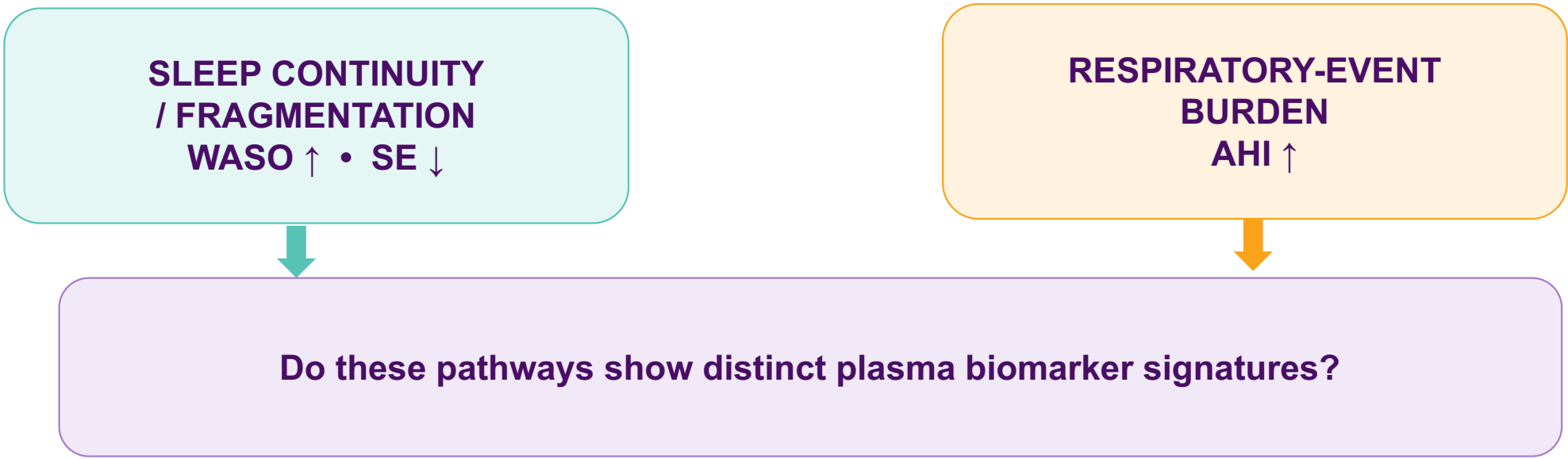


Sleep fragmentation and sleep-disordered breathing mapped onto distinct early AD-related plasma biomarker profiles. WASO higher / sleep efficiency lower tracked amyloid-related signal and NfL independent of AHI, whereas AHI selectively tracked GFAP.

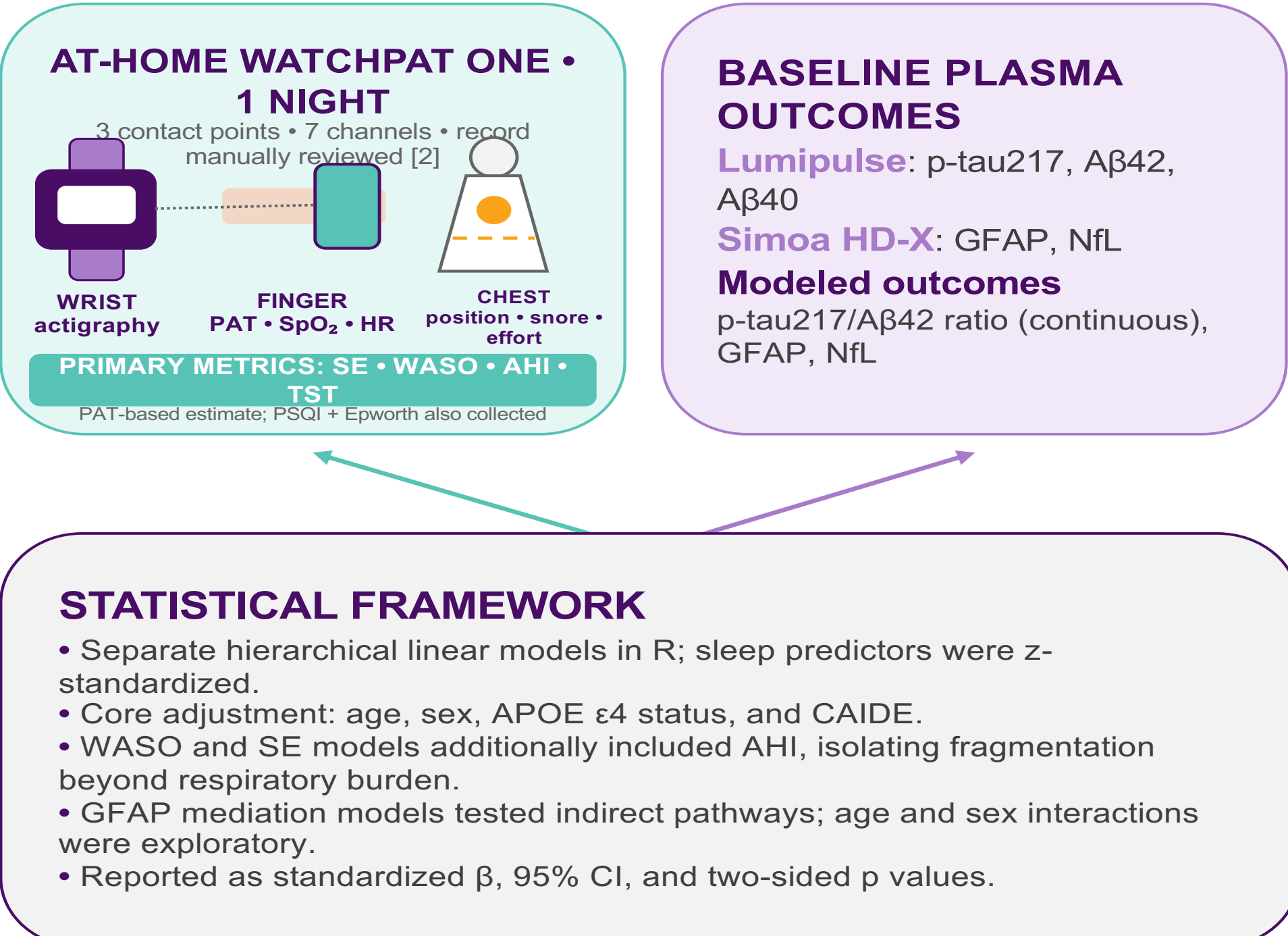
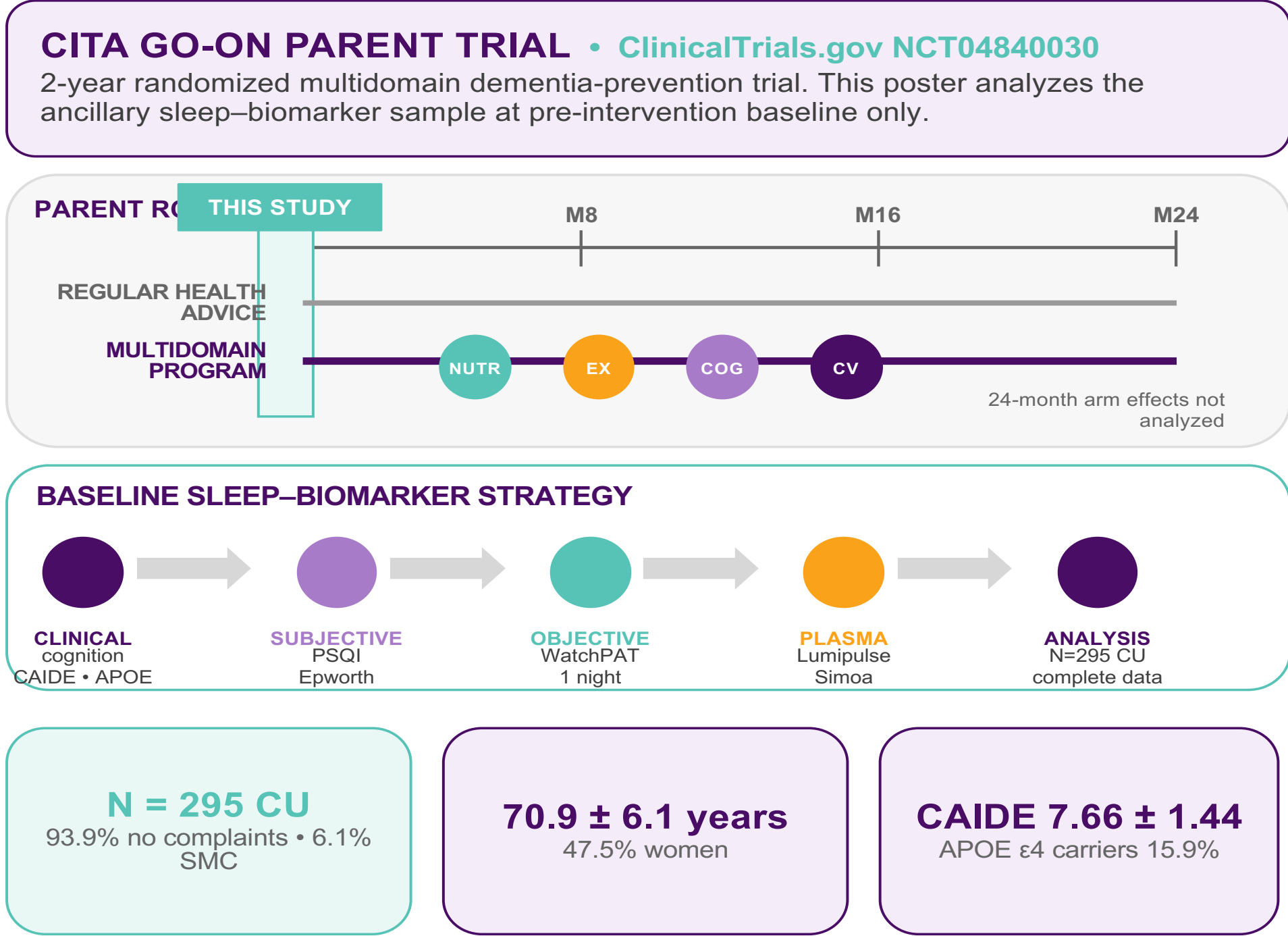
1. INTRODUCTION

KNOWLEDGE GAP
Sleep fragmentation and sleep-disordered breathing often coexist. Fragmentation has been linked to altered proteostasis and neuroaxonal vulnerability, whereas respiratory disturbance may preferentially engage astroglial responses. Few studies have modeled both dimensions simultaneously against plasma amyloid-, glial-, and axonal biomarkers.

OBJECTIVE
Disentangle the independent associations of WASO, sleep efficiency, and AHI with plasma p-tau217/Aβ42, GFAP, and NfL.



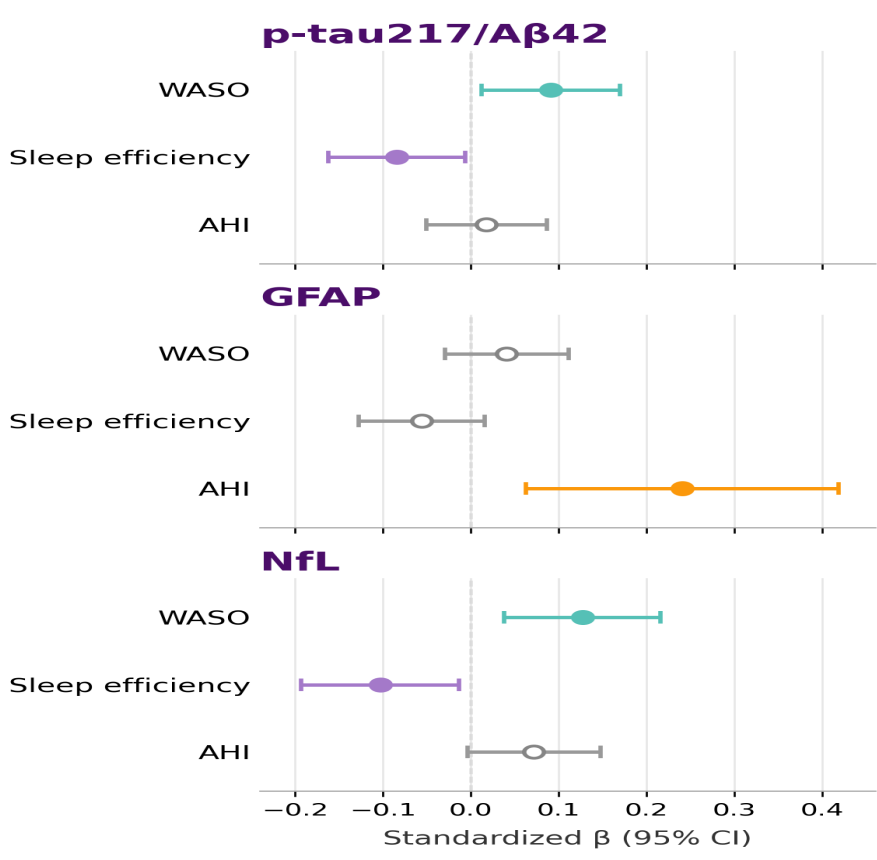
2. METHODS



3. RESULTS

FULLY ADJUSTED BASELINE ASSOCIATIONS

Standardized β (95% CI). Core model: age, sex, APOE ε4, CAIDE; WASO/SE models additionally adjusted for AHI.



FRAGMENTATION SIGNATURE

Concordant WASO and SE associations; independent of AHI
p-tau217/Aβ42: WASO β=.091 (p=.024); SE β=-.084 (p=.034)
NfL: WASO β=.127 (p=.006); SE β=-.103 (p=.025)

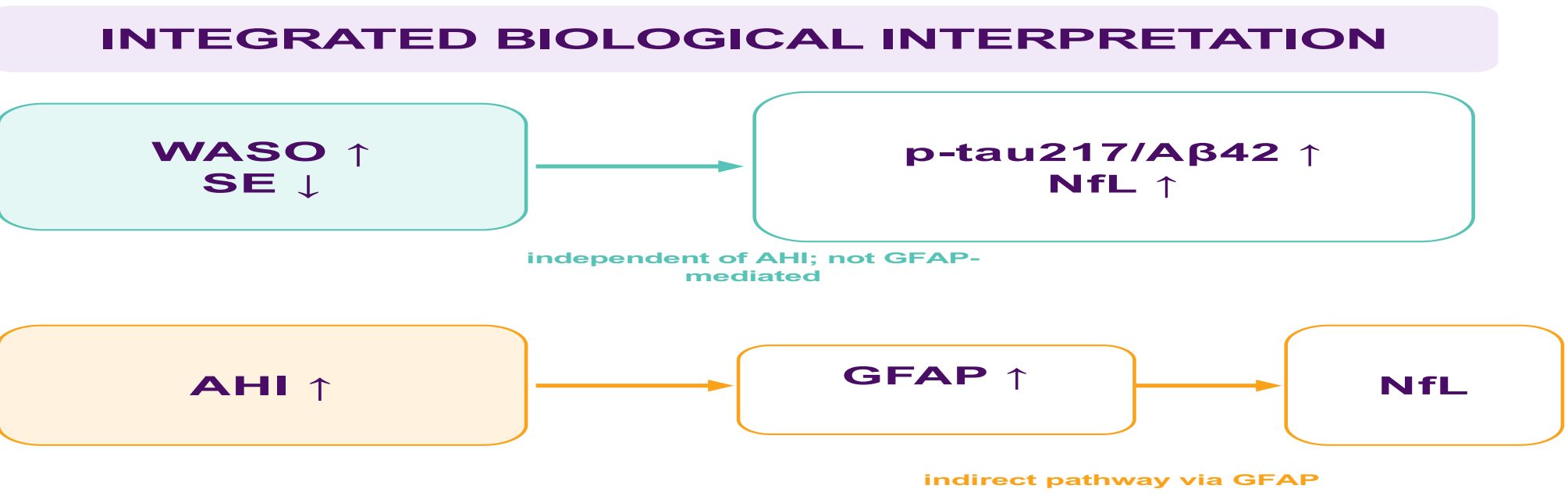
RESPIRATORY SIGNATURE

Selective astroglial association
AHI → GFAP: β=.241 (95% CI .063–.419), p=.008
No p-tau217/Aβ42 signal (p=.61); NfL trend (p=.064)

SPECIFICITY, MEDIATION & MODERATION

Fragmentation→GFAP was non-significant (WASO p=.25; SE p=.13). GFAP mediated AHI→NfL, but not fragmentation→p-tau217/Aβ42. Associations were age-consistent; lower SE showed a stronger GFAP association in women (exploratory).

4. CONCLUSIONS



INTERPRETATION & DISCUSSION

- The findings argue against one interchangeable “poor sleep” pathway.
- Fragmentation tracked an amyloid-related plasma ratio and axonal injury beyond AHI, supporting a distinct non-respiratory signal.
- Respiratory-event burden mapped most strongly to GFAP; its indirect association with NfL is compatible with astroglial involvement.
- Cross-sectional mediation is hypothesis-generating—not causal—and the sex interaction requires replication

NEXT STEP / LIMITATIONS: single-night WatchPAT, residual confounding, and cross-sectional design limit directionality. Longitudinal and intervention studies should test modifiability.

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