

Associations Between Daytime Napping and Longitudinal Tau Accumulation in the Preclinical Alzheimer’s Disease Continuum

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OBJECTIVE

To determine whether self-reported daytime napping duration predicts longitudinal regional tau PET burden and cognitive trajectories in a biomarker-stratified preclinical cohort.

TAKE AWAY

➤ Long nappers have higher tau at every visit across 4.7 years, but the gap does not widen, napping predicts existing tau burden, not the rate of accumulation (all trajectory terms null).

➤ The napping–tau association is amyloid-independent (Aβ+: β=0.056, p=0.007; Aβ–: β=0.053, p=0.038; moderation LRT p=0.959), consistent with tau accumulating in wake-promoting neurons before significant cortical amyloid involvement.

➤ Existing medial temporal tau burden fully mediates the association between habitual long napping and future cognitive decline (indirect: β=–0.203, p=0.032; direct beyond tau: p=0.646).

➤ Reverse causation, not confounding: the signal lives in stable between-person napping patterns (p=0.036), not visit-to-visit fluctuations (p=0.130)

INTRODUCTION

The Preclinical Window: Alzheimer’s disease (AD) pathology accumulates silently for 15–20 years before cognitive symptoms emerge. Developing accessible behavioral markers of this early molecular phase is critical for everyday clinical screening.

The Tau Driver: While β-amyloid (Aβ) accumulates first, neocortical cognitive decline is driven directly by the predictable outward spread of misfolded tau protein from medial temporal lobe (MTL) hubs.

The Sleep Paradox: Longer nighttime sleep is linked to lower amyloid burden. Conversely, habitual long daytime napping (>30 min/day) is linked to increased dementia risk and faster cognitive decline.

The Subcortical Mechanism: This napping paradox points to reverse causation. Tau accumulates preferentially in subcortical wake-promoting nuclei (e.g., Locus Coeruleus), driving neuronal loss and subsequent behavioral hypersomnolence as an early read-out of neurodegeneration.

RESULTS

Long daytime napping (>30 min/day) was associated with significantly higher baseline tau burden in both medial temporal (MTL: β = 0.056, p = 0.007) and neocortical (NEO: β = 0.048, p = 0.042) regions among Aβ+ participants (Table 1).

Long-nappers exhibited consistently higher tauNEO compared to non-nappers across all four longitudinal visits, with parallel trajectories indicating that napping predicts baseline burden rather than the rate of accumulation (Figure 1).

We observed no significant 3-way interaction between time, napping, and amyloid status (tauMTL p = 0.959; tauNEO p = 0.712), suggesting the napping–tau relationship operates independently of Aβ pathology.

Latent growth curve mediation confirmed that baseline tauMTL fully mediated the association between long napping and faster PACC cognitive decline over 4.7 years (indirect effect: β = –0.203, p = 0.032; direct effect: β = 0.056, p = 0.646) (Figure 2).

Decomposition of napping via Mundlak centering revealed that only the stable between-person trait (not visit-to-visit state fluctuations) predicted tauMTL burden (β = 0.012, p = 0.036), supporting reverse causation where tau-mediated degeneration of wake-promoting neurons drives the long-napping phenotype (Table 2).

METHODS

Study Population: We analyzed n = 437 participants (Aβ+ and Aβ–) from the A4 Study (Anti-Amyloid Treatment in Asymptomatic Alzheimer’s) across 240 weeks (4.7 years).

Behavioral Assessment: Daytime napping duration was assessed at baseline and longitudinal visits via the Habitual Napping Questionnaire. Participants were stratified into Non-nappers (0 min), Short-nappers (1–30 min), and Long-nappers (>30 min/day).

Pipeline: Medial temporal (MTL) and neocortical (NEO) tau SUVRs were acquired at four longitudinal time points. The Preclinical Alzheimer’s Cognitive Composite (PACC) was used to measure longitudinal cognitive performance.

Statistical Analysis: To account for exact longitudinal intervals, time was modeled continuously in weeks (ADURW). We used Latent Growth Curve Mediation (LGCM) models in *lavaan* to estimate the mediation pathways. Mundlak centering was applied to decompose napping into stable between-person traits and within-person state fluctuations, formally separating the influence of pathology-driven napping from napping-driven pathology.

Table 1 Primary Categorical Model: Napping → Tau Burden (LME)

Predictor	Estimate	95% CI	p-value
tauMTL — Aβ+			
Long-napper vs Non-napper	0.056	[0.015, 0.097]	0.007
time × Long-napper	0.002	[–0.008, 0.013]	0.669
tauNEO — Aβ+			
Long-napper vs Non-napper	0.048	[0.002, 0.094]	0.042
time × Long-napper	0.016	[–0.003, 0.034]	0.090 ^a
tauMTL — Aβ–			
Long-napper vs Non-napper	0.053	[0.003, 0.102]	0.038
time × Long-napper	–0.002	[–0.022, 0.017]	0.813

Note: All models adjusted for age, sex, APOE-ε4, and education. Short napper coefficients were non-significant across all models

Table 2 Comparison of between-person and within-person effects of daytime napping on baseline tau burden and longitudinal tau accumulation

	tauMTL		tauNEO	
Term	Estimate	p-value	Estimate	p-value
Between-person trait (level)	0.012	0.036	0.008	0.218
Within-person state (level)	0.002	0.130	0.001	0.796
Trait × time (slope)	–0.001	0.722	0.003	0.315
State × time (slope)	–0.001	0.197	0.001	0.474

Note: MTL = medial temporal lobe; NEO = neocortical.

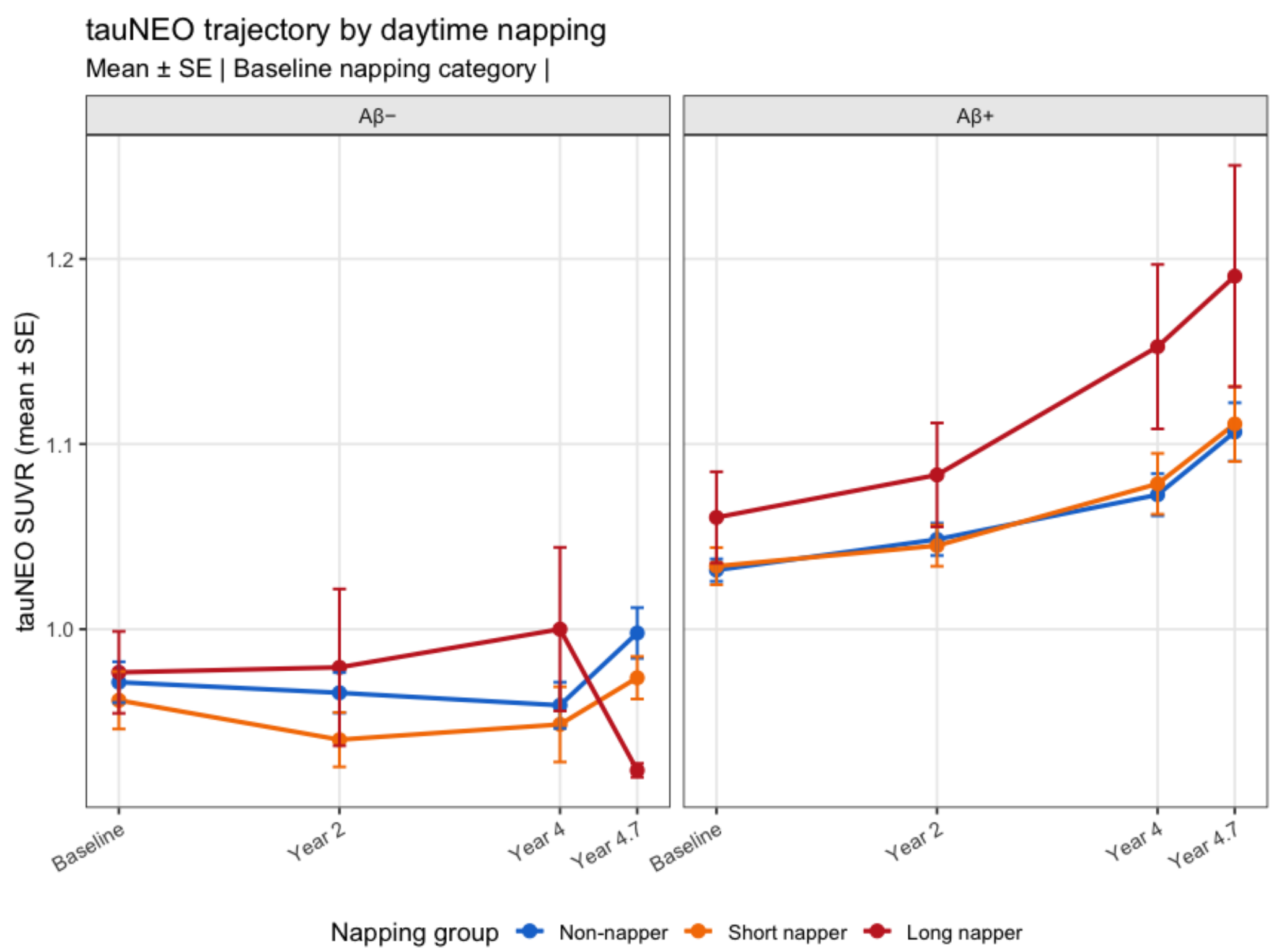
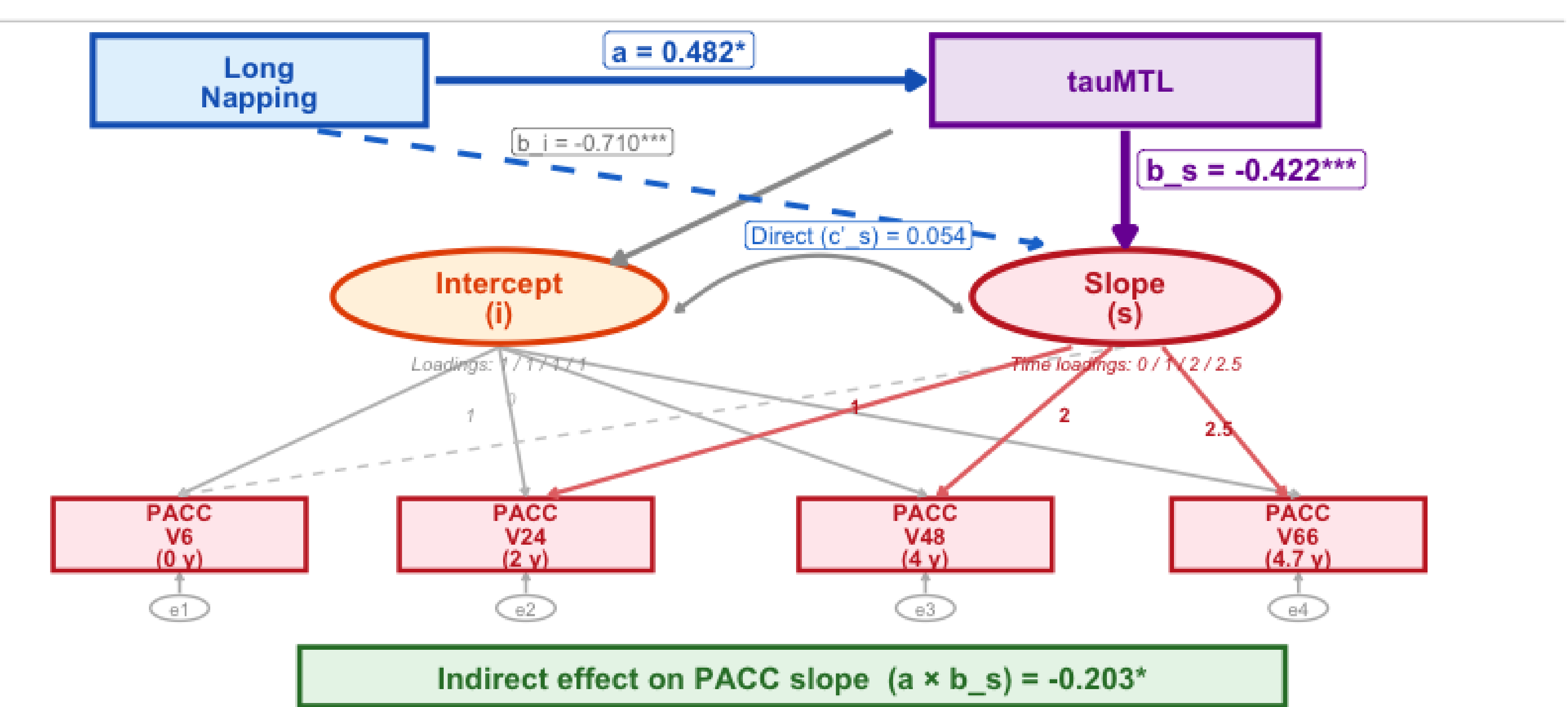


Figure 1 Neocortical tau (tauNEO) trajectories by baseline napping category and amyloid status. Points represent unadjusted means ± standard error at each visit.

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A Long Napping → tauMTL → PACC Trajectory



B Long Napping → tauNEO → PACC Trajectory

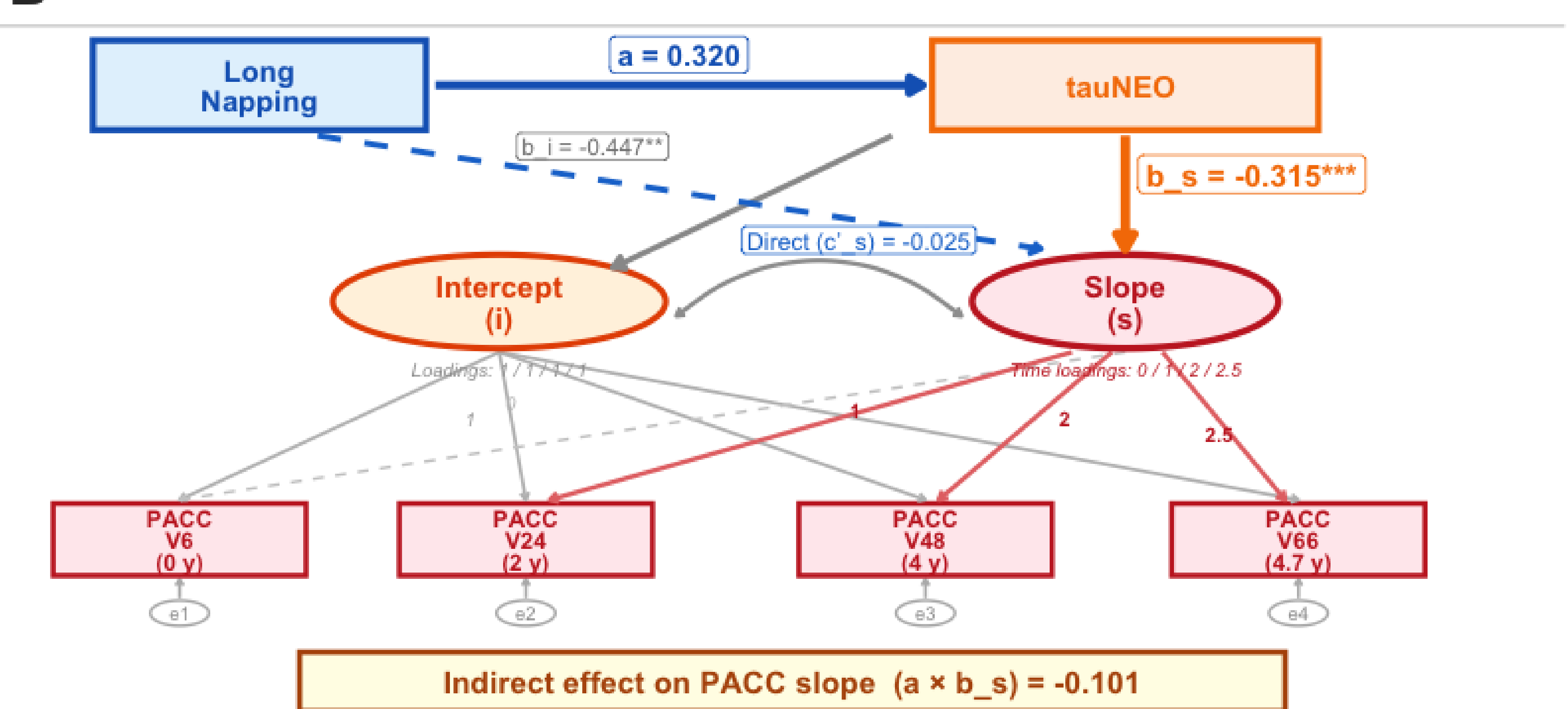


Figure 2 Medial temporal tau mediates the association between habitual long napping and rate of cognitive decline. Latent growth curve mediation models in Aβ+ participants (n=383) over 4.7 years. Panel A: tauMTL (entorhinal cortex + amygdala)