



Network Analysis Reveals REM Sleep Latency and Tau as Key Bridges Linking Sleep Architecture, Alzheimer’s Biomarkers, and Cognitive Function



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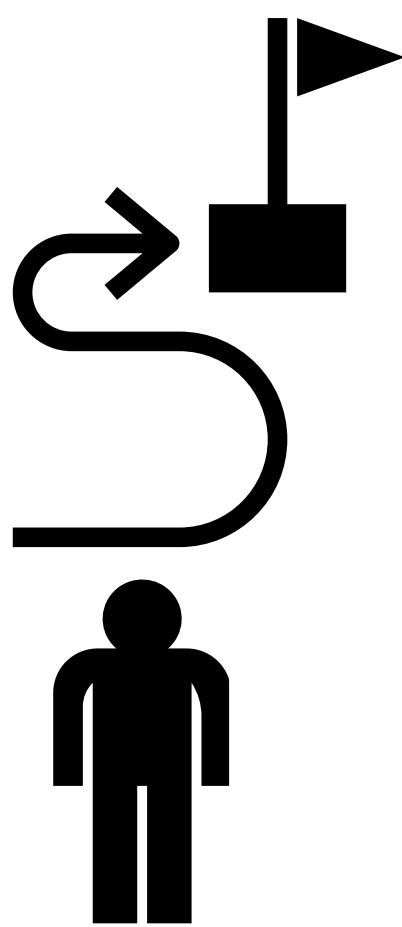
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Background

- ❑ Sleep disturbances are common across the Alzheimer’s disease (AD) continuum.
- ❑ Sleep architecture, AD and related dementias (ADRD) biomarkers, and cognition are usually analyzed separately.
- ❑ It remains unclear whether sleep relates to cognition directly or through biomarker-linked pathways.

Objective

To identify conditional association structure linking sleep architecture, ADRD biomarkers, and cognitive performance, and to identify cross-domain connector nodes.

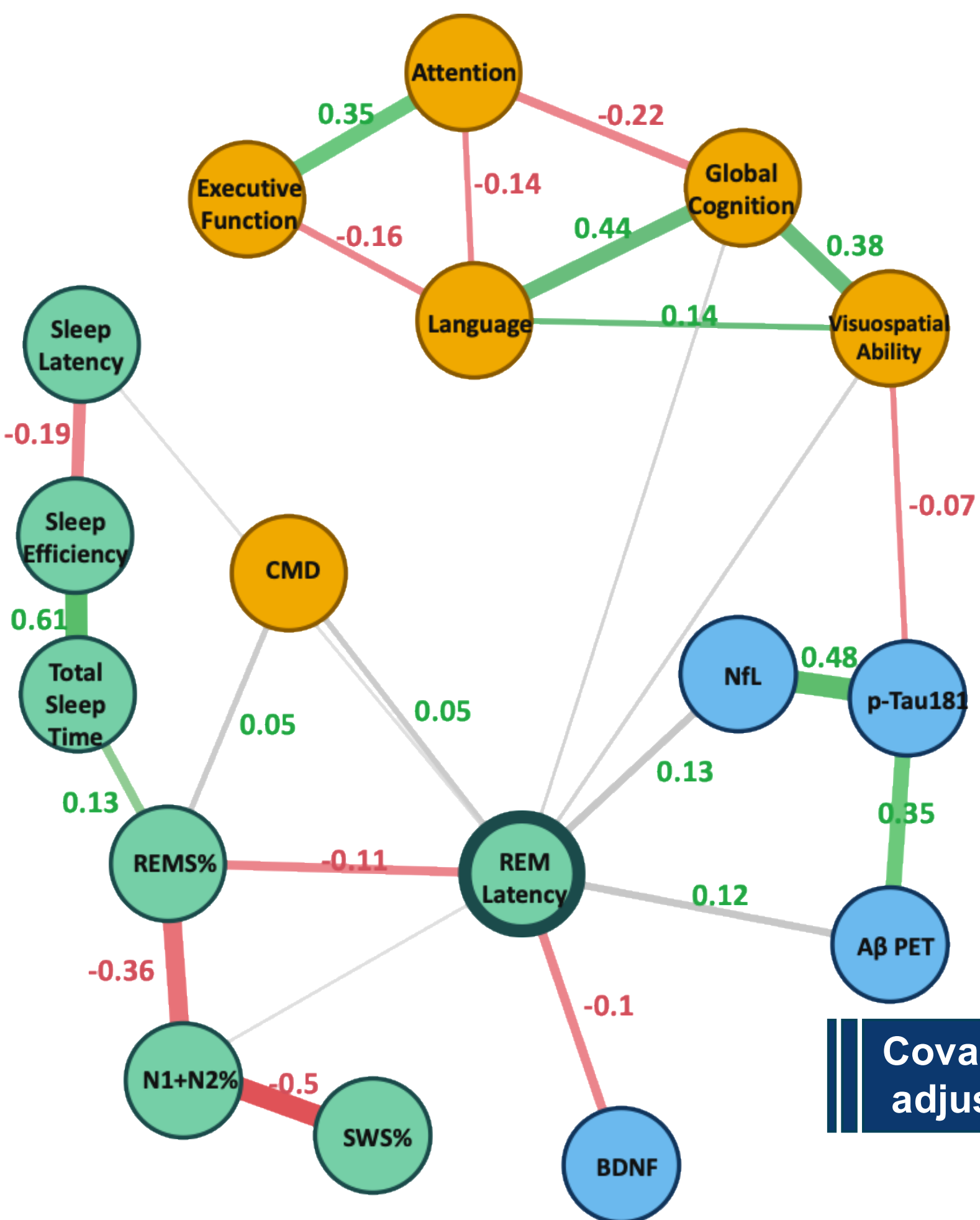
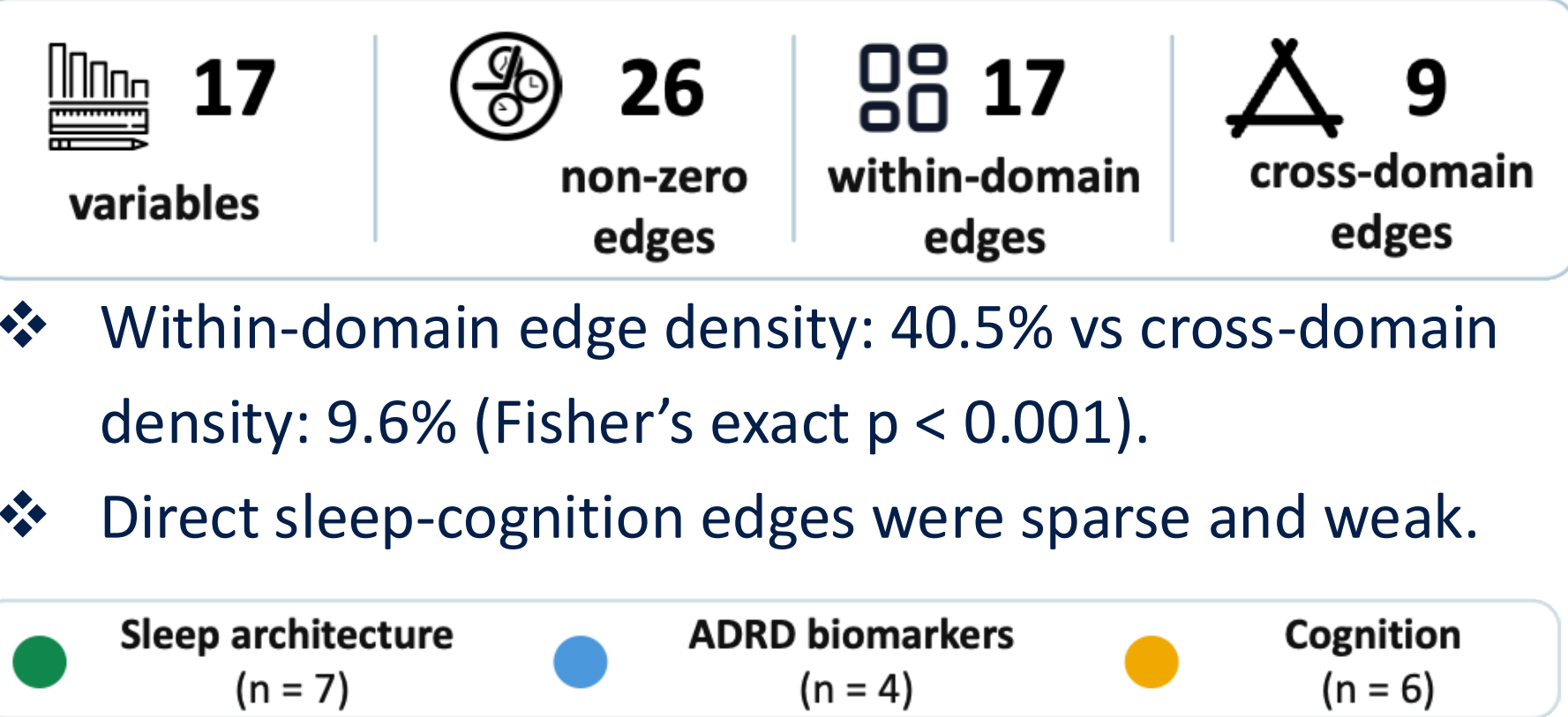


Take-Home Message

- ❖ After conditioning on ADRD biomarkers, sleep and cognition were only weakly directly connected.
- ❖ REM sleep latency was the main bridge linking sleep architecture to biomarker variation.
- ❖ p-tau181 emerged as the primary biomarker linking REM sleep latency to cognitive performance.

Main Results

1 Network organization

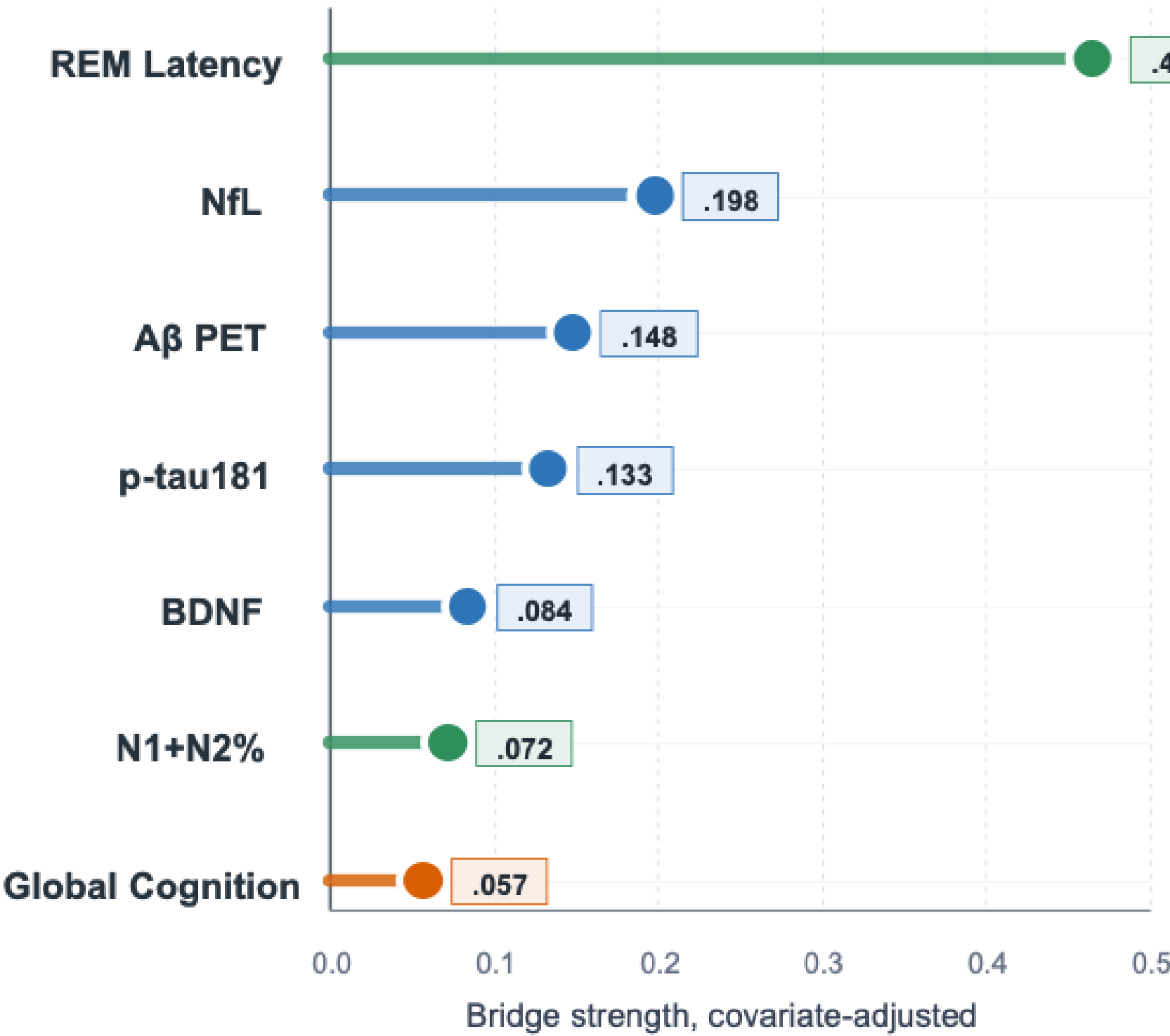


2 REM sleep latency

Primary cross-domain connector:

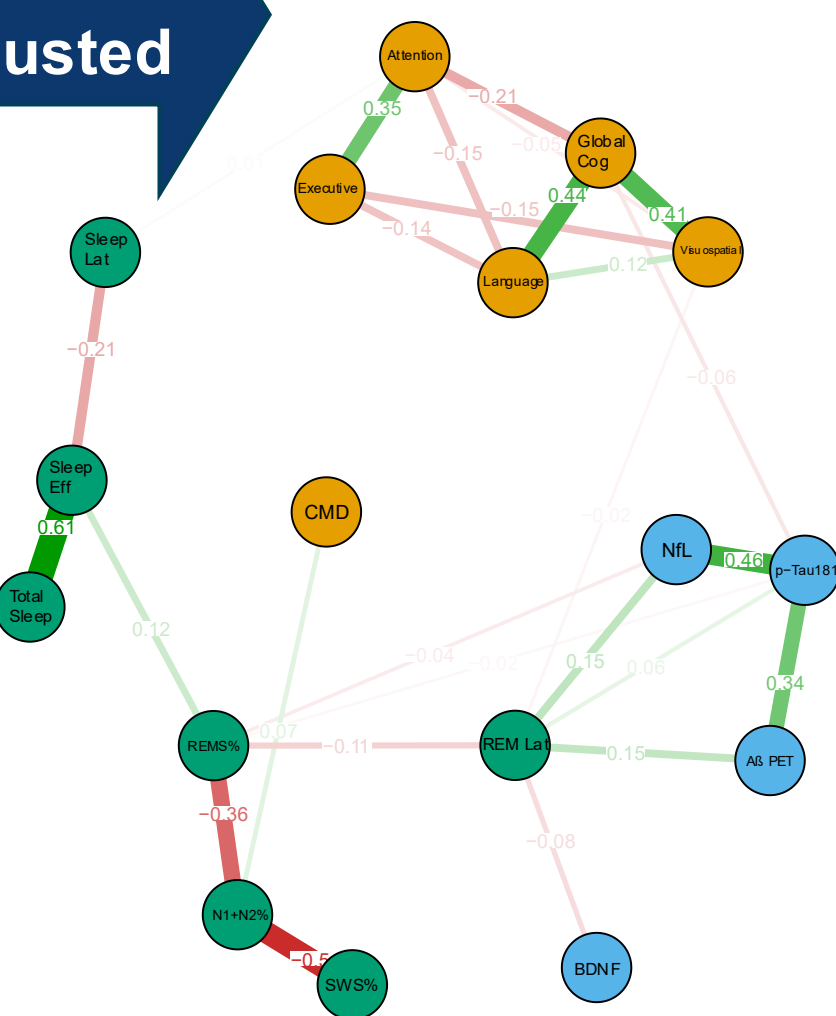
- ❖ Highest bridge strength among all nodes: 0.387
- ❖ Next sleep node: 0.053
- ❖ Partial correlations from REM sleep latency: NfL $r = 0.134$; Aβ PET $r = 0.119$; BDNF $r = -0.105$

3 Bridge strength



- ❖ REM sleep latency was the top cross-domain connector.
- ❖ Biomarker-related connectors ranked next: NfL, Aβ PET, p-tau181, and BDNF.
- ❖ The next sleep node, N1+N2%, showed much weaker bridge strength.

4 Robustness



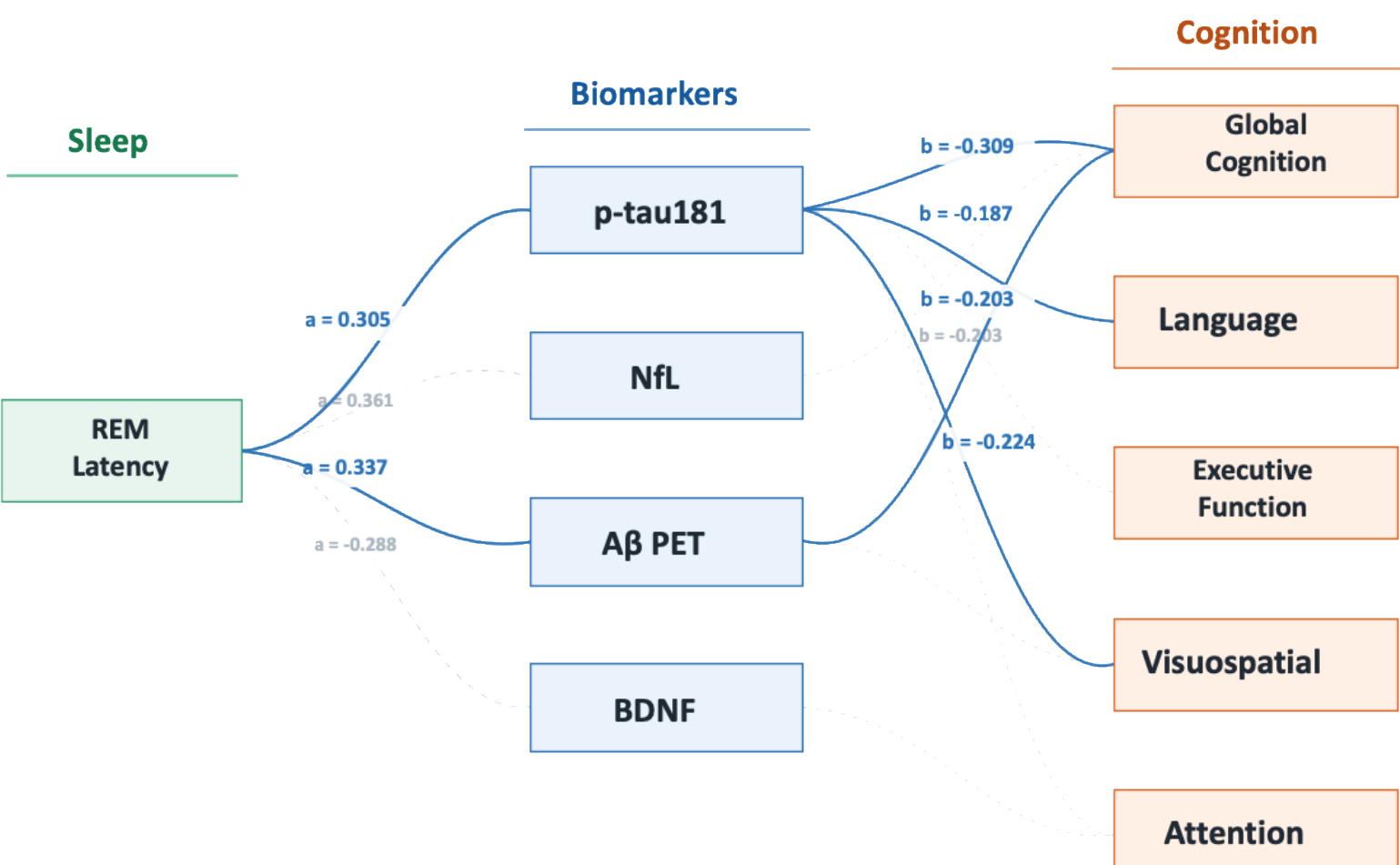
- ❖ Covariate adjustment did not materially alter the network structure.
- ❖ REM sleep latency remained the leading cross-domain connector.
- ❖ Bridge ranking was preserved across sensitivity analyses.



KEY FINDING

Sleep and cognition were weakly connected directly; REM sleep latency linked sleep to biomarkers, and p-tau181 linked biomarkers to cognition.

Exploratory Mediation analysis



Pathway	Indirect effect	% mediated
• REM Lat → p-tau181 → Global Cognition	$ab = -0.094$	(86%)
• REM Lat → p-tau181 → Language	$ab = -0.057$	-
• REM Lat → p-tau181 → Visuospatial	$ab = -0.068$	(44%)
• REM Lat → Aβ PET → Global Cognition	$ab = -0.069$	(62%)

Tau as the Primary Mediator

- ❖ p-tau181 mediated the relationship between REM latency and multiple cognitive domains.

Strongest Effect on Global Cognition

- ❖ Tau pathology explained **86%** of the REM latency–global cognition association.

Amyloid Also Plays a Role

- ❖ Aβ PET mediated the association with global cognition, accounting for **62%** of the total effect.

Selective Cognitive Vulnerability

- ❖ Mediation effects were observed for **global cognition, language, and visuospatial function**, but not executive function or attention.

Methods

Population

- ❖ Cross-sectional study of 98 adults across the AD continuum.
- ❖ 21 cognitively normal, 34 mild cognitive impairment, and 43 Alzheimer’s disease.
- ❖ Mean age 70.9 years; 55.1% female.
- ❖ Overnight polysomnography to quantify sleep architecture.

Measures

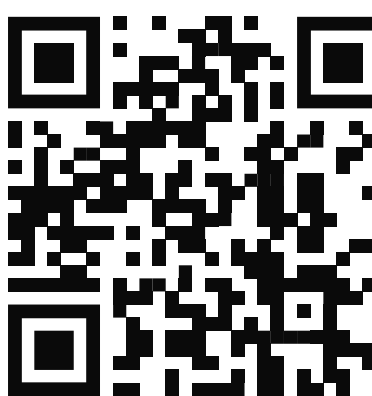
- ❖ Network communities were predefined as sleep architecture, ADRD biomarkers, cognition, and affective symptoms.
- ❖ Plasma p-tau181, NfL, and BDNF Amyloid-β PET standardized uptake value ratio.
- ❖ Multidomain cognitive and affective assessments.

Statistical Analysis

- ❖ Estimated a regularized partial correlation network using a Gaussian graphical model.
- ❖ Edges represent conditional associations after accounting for all other variables.
- ❖ Bridge centrality was used to identify cross-domain connector nodes.

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