

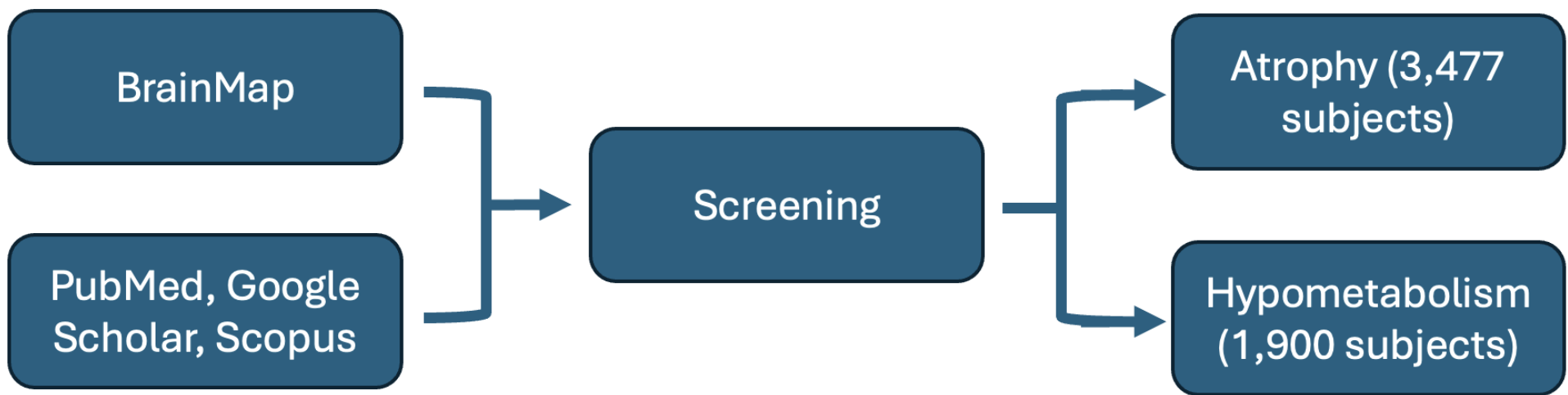
Introduction

- The **Amyloid/Tau/Neurodegeneration** biomarker framework is used for pathological profiling of Alzheimer's disease (AD).
- Under this framework, **neurodegeneration** encompasses both **atrophy** and **hypometabolism**.
- However, there is preliminary evidence that atrophy and hypometabolism are **spatially and temporally distinct**, suggesting **different underlying pathologies**.
- This study:
 - 1) Uses **large-scale meta-analytic analyses** to characterize and compare **regional and network patterns** of atrophy and hypometabolism.
 - 2) Evaluates **network model fit** in a pilot sample and identifies **edge-level differences** between AD and cognitively normal groups.

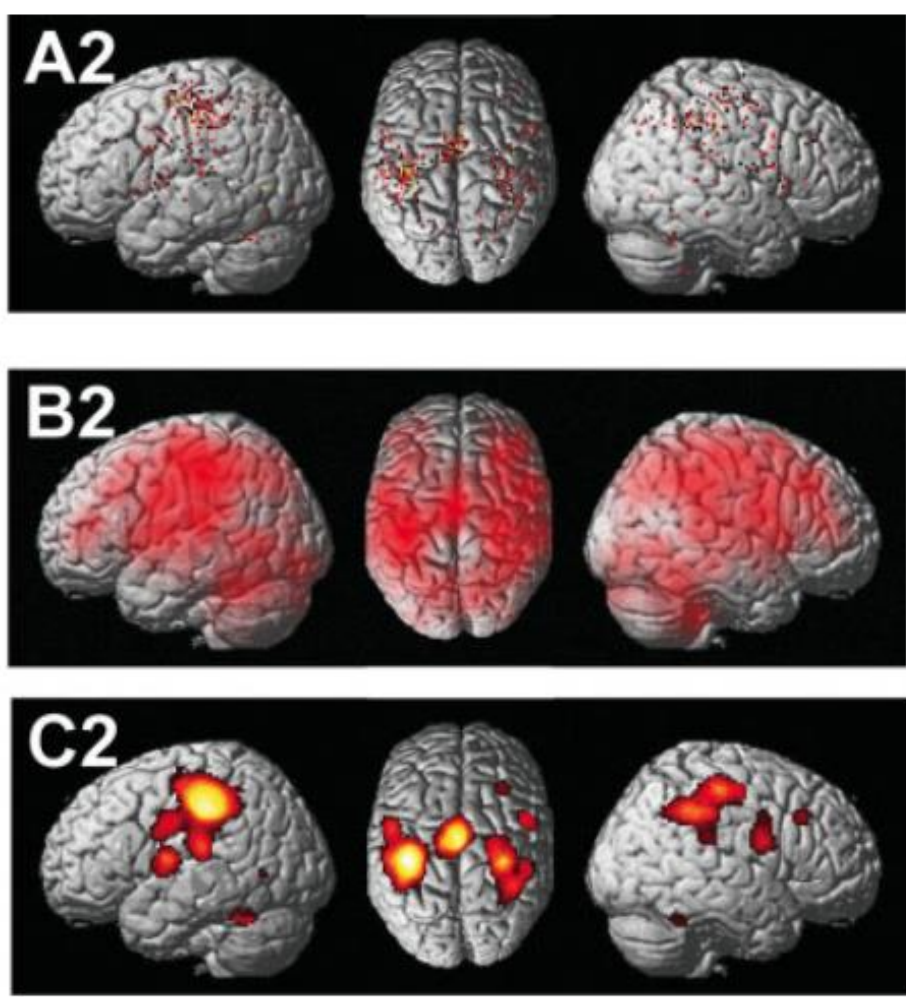
Methods & Results

Goal 1: Characterize regional changes

A. Gather data



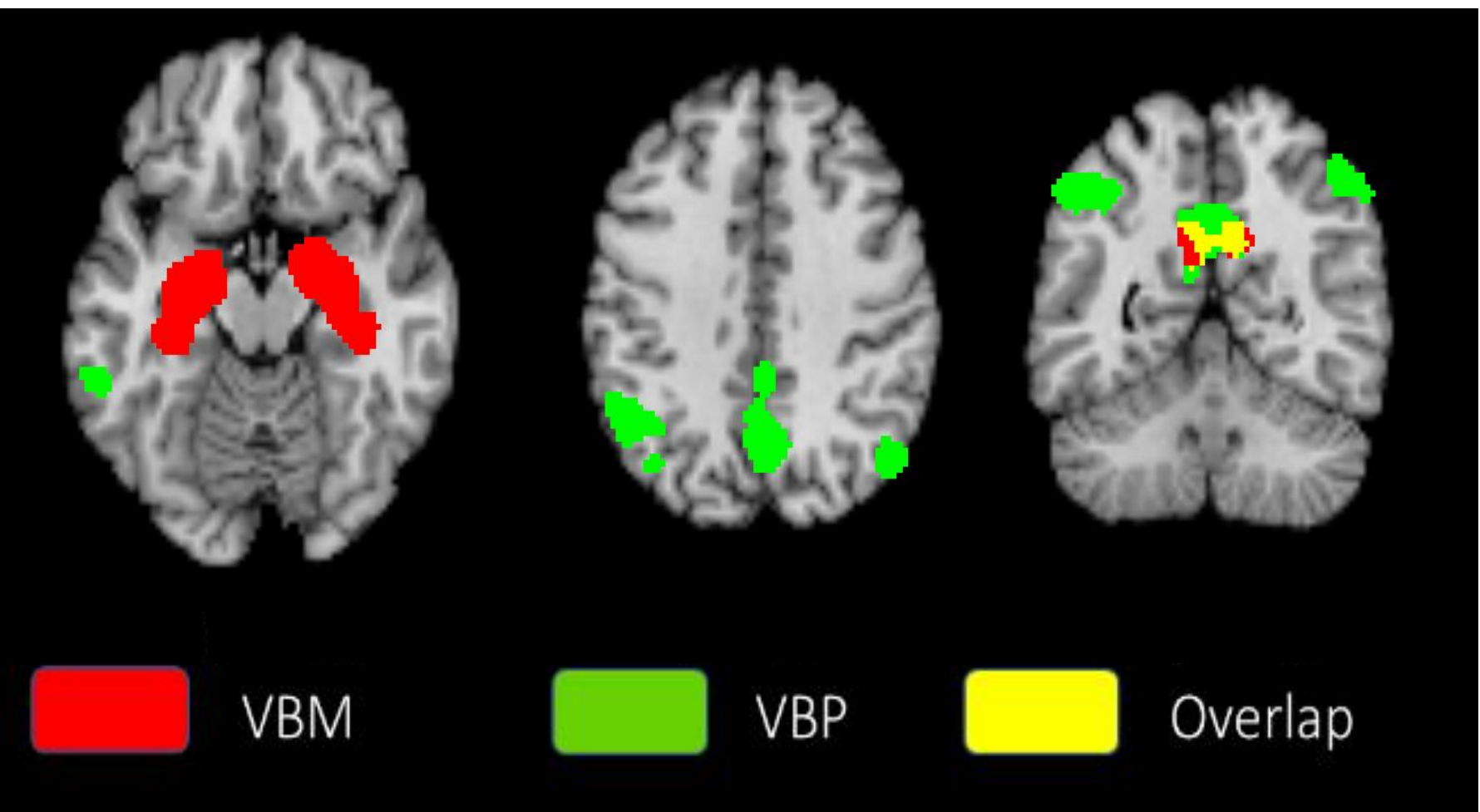
B. Identify regions of convergence between independent studies



- Activation likelihood estimation (ALE) - identify cross-study convergence** of brain alteration patterns.

Eickhoff, 2009

Finding 1: Atrophy & hypometabolism patterns are dissociated



VBM (atrophy) – bilateral hippocampus, posterior cingulate/precuneus, thalamus, insula, uncus

VBP (hypometabolism) – cingulate gyrus/ precuneus/posterior cingulate, inferior parietal lobule, inferior-middle temporal gyrus

Overlap: 4.6% VBM regions; 7.4% VBP regions

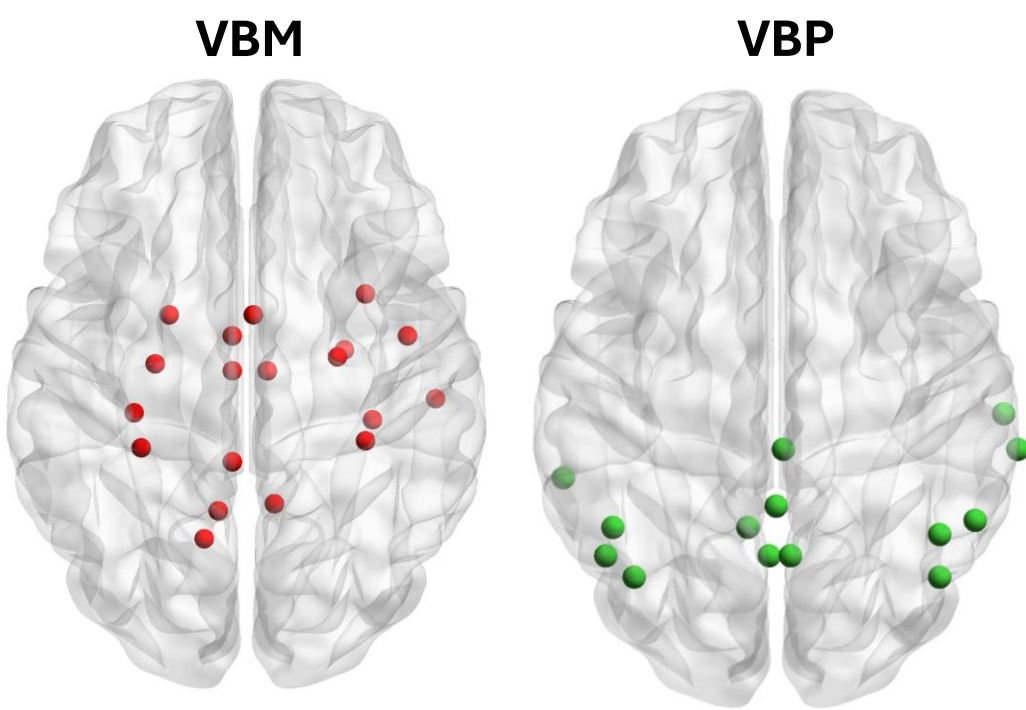
Different brain regions are vulnerable to atrophy vs hypometabolism.

Methods & Results

Goal 2: Characterize network changes

A. Extract nodes

- From ALE local maxima
- VBM: 8 mm diameter
 - 19 nodes
- VBP: 12 mm diameter
 - 14 nodes



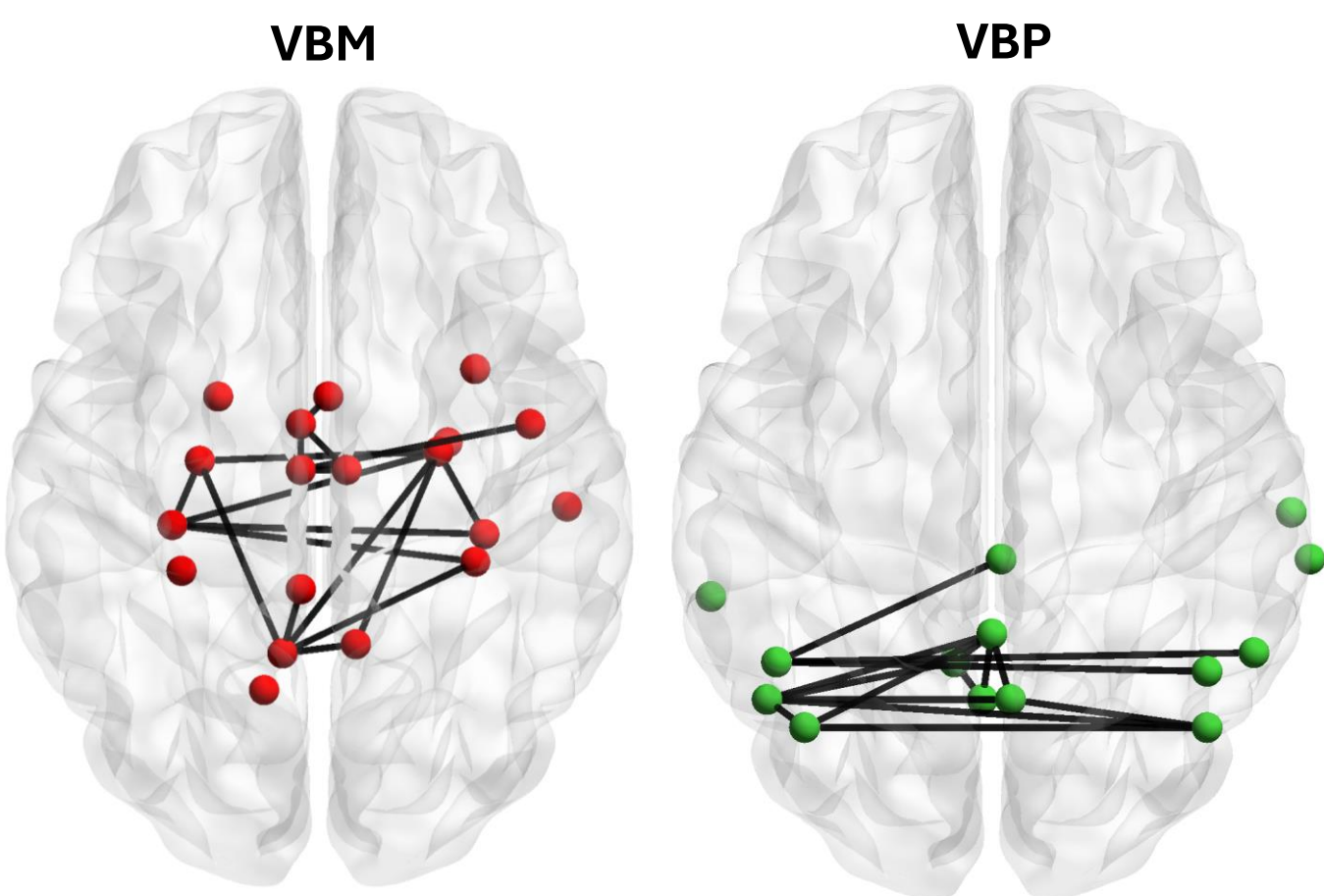
B. Identify edges

- BrainMap healthy task-activation data (100,000+ subjects)

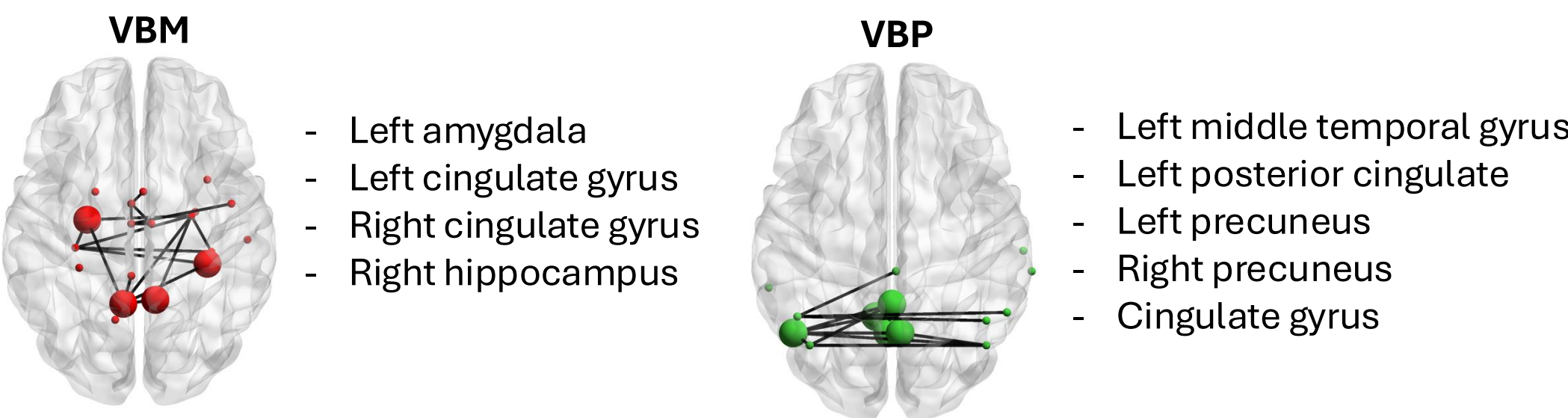
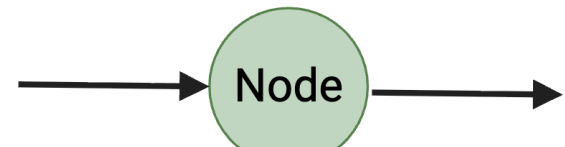
When node X is activated... → What other regions are co-activated? $P < 0.01$

Finding 2: Atrophy & hypometabolism occur in a network-based manner

VBM: 13/19 nodes connected
VBP: 11/14 nodes connected



Node degree (edges in + edges out) was used to determine network hubs



1. VBM and VBP patterns form distinct networks
2. VBM hubs are located in the medial temporal lobe and bilateral cingulate gyrus; VBP hubs are components of the posterior DMN

Goal 3: Evaluate model fit and edge-level differences

A. Data

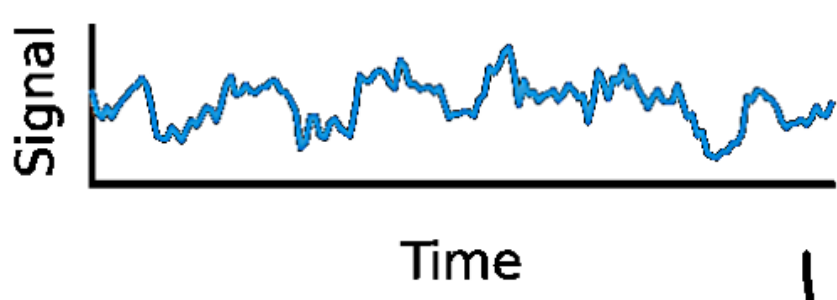


	Alzheimer's Disease	Cognitively Normal
N	11	11
Sex (M/F)	3/8	6/5
ApoE status	7 E3/E4; 2 E4/E4; 2 unavailable	5 E3/E3; 2 E3/E4; 3 E2/E3; 1 E4/E4

- Resting-state fMRI and T1 structural MRI
- Standard preprocessing of images (fMRIprep, ICA post-AROMA, FSL)

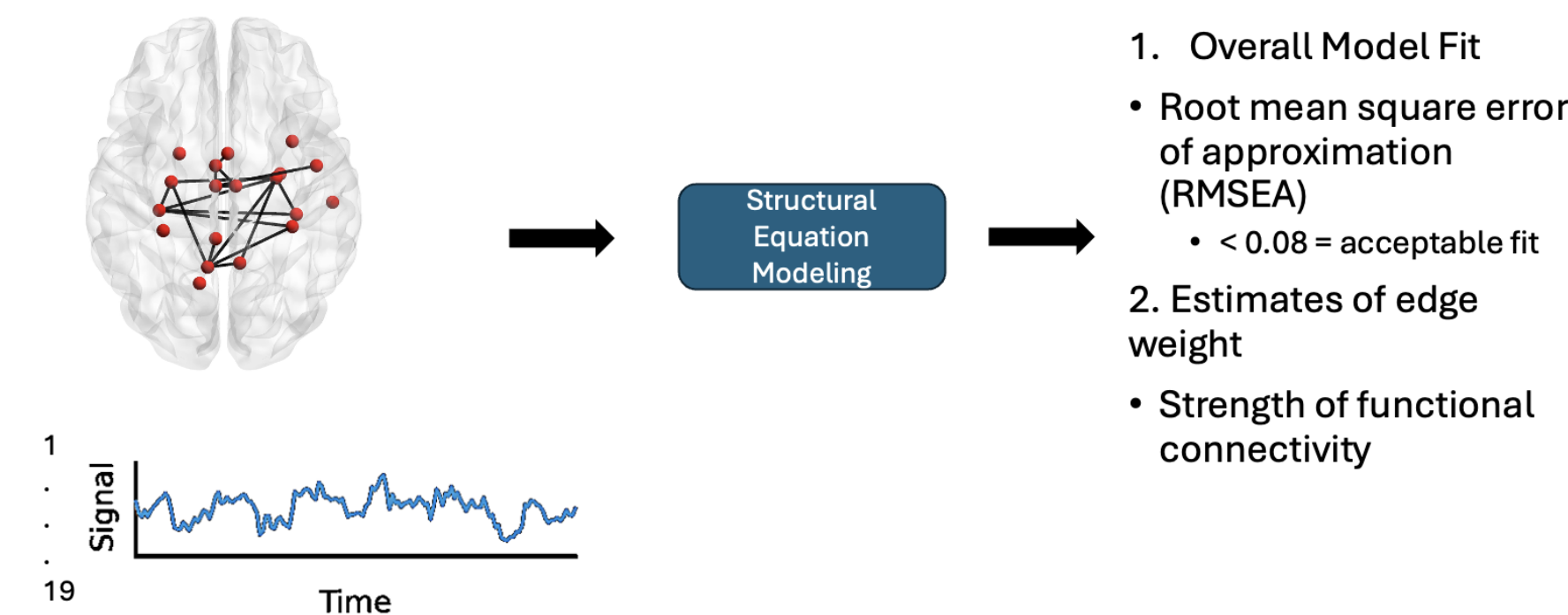
B. Region of Interest (ROI) sampling

- Mean time-series data was extracted from VBM and VBP nodes



Methods & Results

C. Structural equation modeling (SEM) was used to assess model fit and path-level differences



Finding 3: VBM model demonstrated acceptable fit, with both increased and decreased connectivity. VBP model demonstrated poor model fit.

1. VBM model – 13 nodes, 16 edges

- RMSEA = 0.067 → acceptable model fit
- Decreased connectivity:

- R_PH_ant → L_PH_ant
- L_CG_preC → R_CG_preC
- L_T_VA → L_T_MD

- Increased connectivity:

- AC_cau → L_T_VA
- L_CG → R_CG_PreC
- L_T_VA → R_T_MD

- Interhemispheric and hub regions were preferentially affected

2. VBP model – 11 nodes, 15 edges

- RMSEA = 0.136 → poor model fit
- Path-level differences could not be evaluated

Conclusions

- Atrophy and hypometabolism patterns are **spatially distinct**.
- Both atrophy and hypometabolism occur in **network-based** patterns, which are distinct from each other.
- VBM model demonstrated acceptable model fit, with **interhemispheric connections and hub regions** preferentially affected.
- VBP model demonstrated poor model fit.

Overall: This work developed network models and tested them in a pilot sample. Results support continued **model optimization** and validation in **larger cohorts**, with the long-term goal of serving as quantitative diagnostic and prognostic tools for AD.

Acknowledgments

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References

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