Medial temporal lobe (MTL) – default-mode network (DMN) functional connectivity disruption in the early stages of the progression of Alzheimer's disease in a multimodal ADNI3 MP-RAGE and EPI-BOLD *Advanced* cohort

#67435

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Text

Resting-state functional connectivity (rsfMRI) as a biomarker of the progression of Alzheimer's Disease

- Temporally advanced with respect to MRI structural biomarkers

ADNI Basic cohort (N=49)

- Age-matched ($p=0.37$)
- Education-matched ($p=0.65$)
- Gender-matched ($p=0.29$)
- Cognitively normal (CN, N=14)
- Significant memory concern (SMC, N=15)
- Early mild cognitive impairment (EMCI, N=11)
- Late MCI (LMCI, N=9)

Cross-sectional same-session analysis

- T1 structural MRI
- Resting-state functional connectivity

Does rsfMRI "see" where MRI does not (yet) "see" evidence of Alzheimer's Disease stages?

Sequential hybrid *a priori* and data-driven method to identify AFNI-processed rsfMRI region-of-interest (ROI) anchor and target pairs [1]

- Single-hemisphere anchor ROI regions
  - Medial Temporal Lobe (MTL)
  - Thalamus (THAL)
  - Amygdala (AMYG)
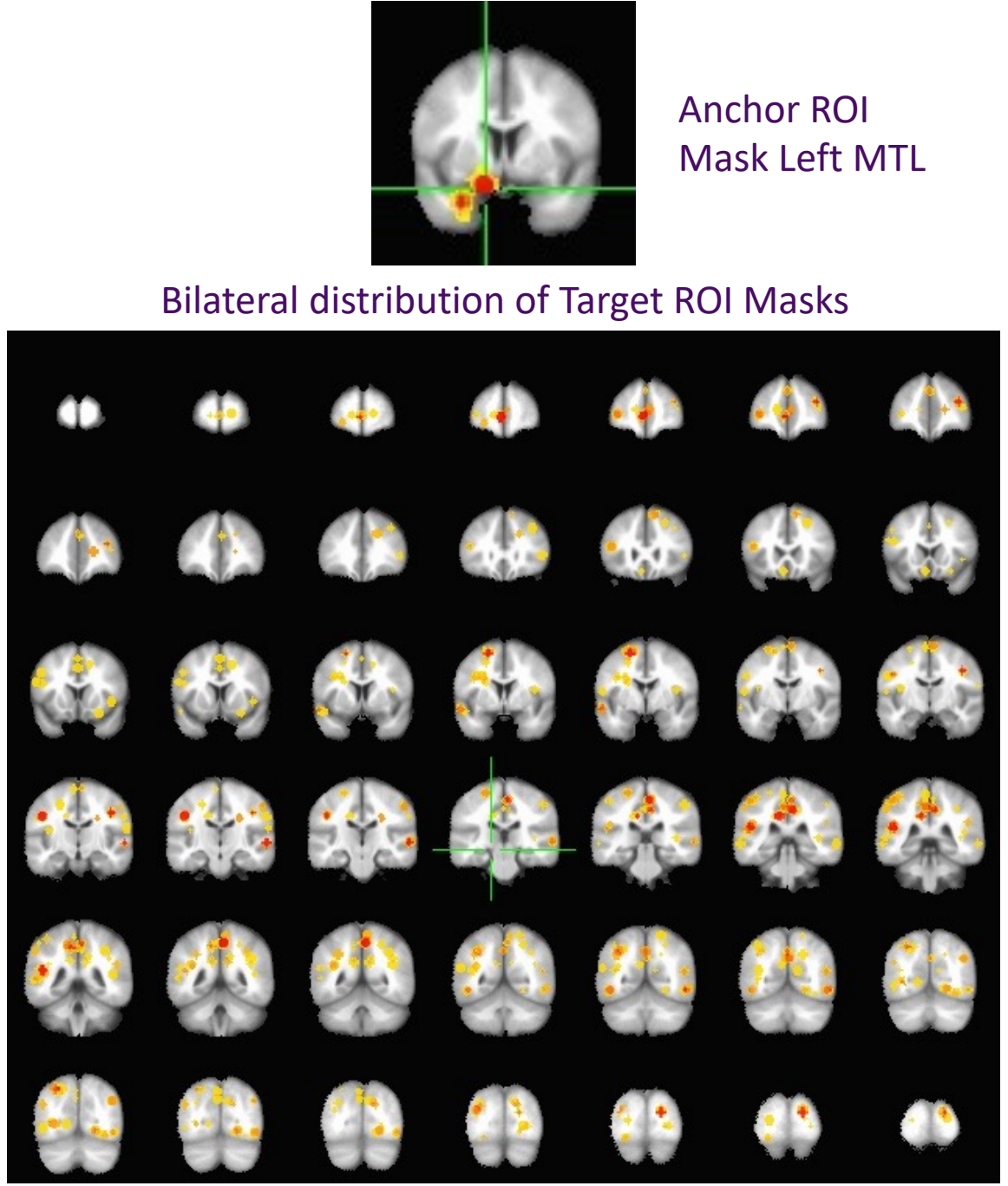 - Nucleus Accumbens (ACC)
  - Substantia Nigra (SN)
- Target ROI regions
  - Bilateral, cortical
  - Subcortical

Freesurfer 7-processed MRI

- Confirm progression across Alzheimer's Disease stages in the cohort
- Observe adjacent-stage Alzheimer's Disease stages where MRI biomarkers (e.g., (sub)cortical thickness) **not** statistically significant (e.g., CN-SMC, SMC-EMCI)

Representative result: for EMCI-CN left-hemisphere anchor ROI in MTL (*top*) targets (bottom) bilaterally not uniformly associated with DMN (*FDR-corrected, q=0.005*):

Anchor ROI Mask Left MTL

Bilateral distribution of Target ROI Masks

Anchor ROIs in MTL (see Results) and multiple subcortical regions such as thalamus, amygdala, and nucleus accumbens (not shown) identified bilateral target ROIs that were predominantly, but not uniformly associated with DMN.

For a given ROI pair

- Progression across Alzheimer's Disease stages was not uniformly in the direction of *hypocorrelation*

Across ROI pairs

- Progression across Alzheimer's Disease stages showed a mixture of hyper- and hypo-correlation, with a preponderance of *hypercorrelation* in the earliest stages

ROI pair identification procedure parameters (e.g., spatial smoothing, cluster sizes, etc.) may require further tuning.

The multi-modal analytics-ready dataset is available for sharing or collaboration free of charge to interested researchers. Contact Author.

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[1] Grajski, K. A., Bressler, S., and ADNI. (2019). *Neuroimage Clin.* 2019;23:101860. https://doi.org/10.1016/j.nicl.2019.101860

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