Integrating Multimodal Neuroimaging Features to Predict Working Memory and Psychiatric Disability

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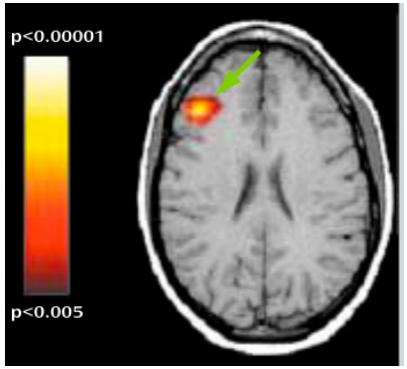
Why focus on working memory capacity (WMC)?

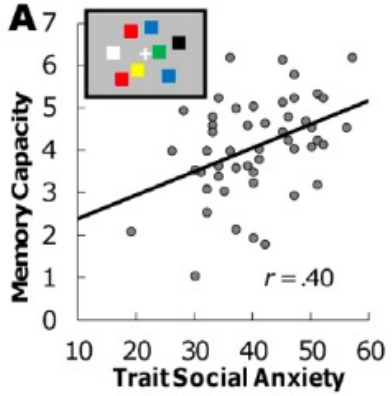
- WMC is positively correlated with other higher order cognitive ability:
  - Fluid intelligence (Chuderski et al., 2012; Unsworth et al, 2014; Unsworth et al., 2015)
  - Reasoning ability (Kyllonen and Christal, 1990)
  - Procedural and declarative learning (Kyllonen and Stephens, 1990)

Why focus on working memory capacity (WMC)?

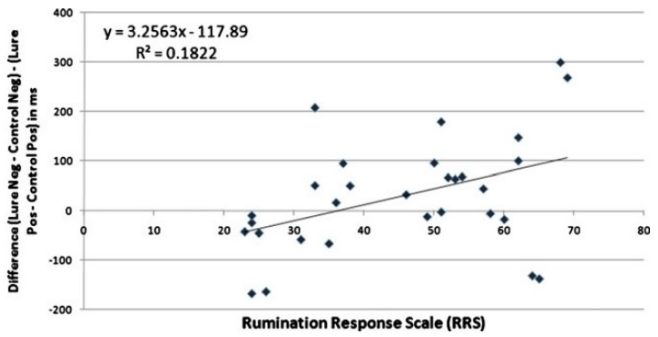
- WMC is also been negatively correlated with dysfunction in psychiatric conditions



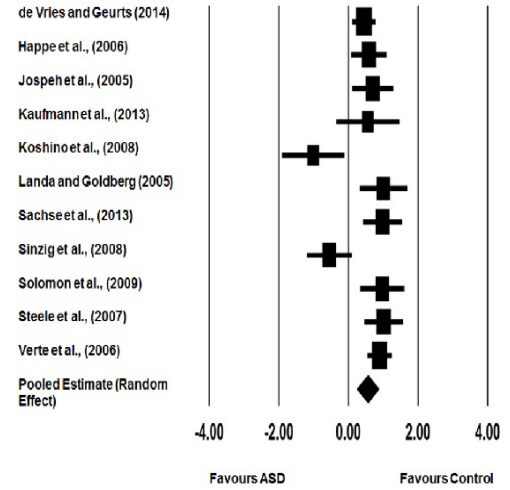
Schizophrenia
(Perlstein et al., 2001)



Anxiety
(Moriya & Sugiura, 2012)



Depression
(Berman et al., 2011)



Autism Spectrum Disorder
(Habib et al., 2019)

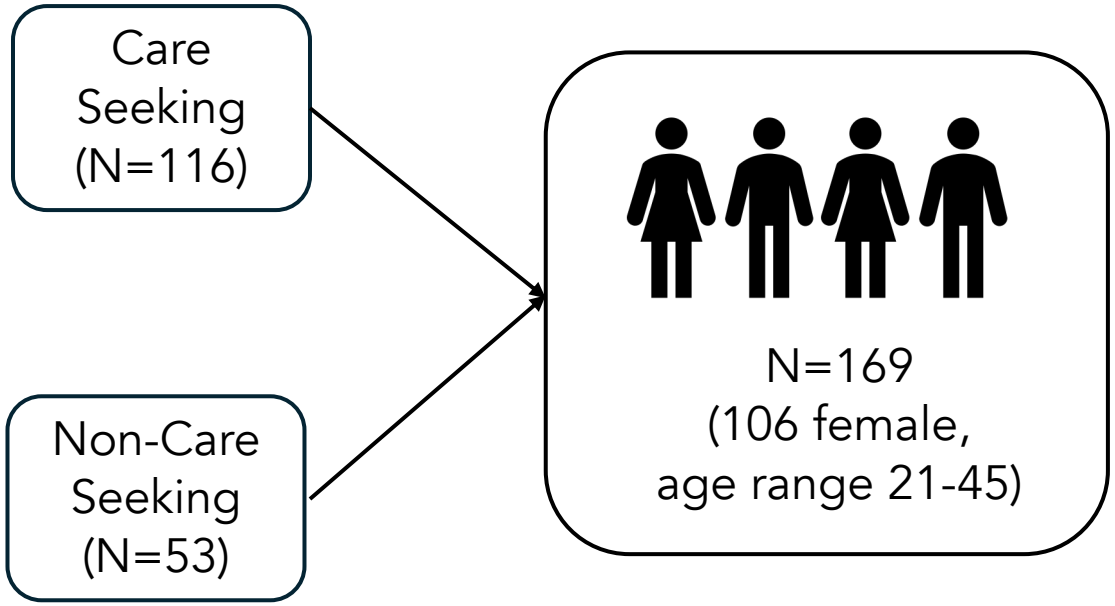
➢Most studies only look at one psychiatric population at a time

Research questions

- What neuroimaging features predict individual differences in working memory capacity (WMC) and performance?

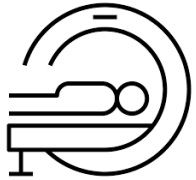
- Can neuroimaging features that predict individual differences in WMC *also* predict transdiagnostic psychiatric disability?

Participants



Behavioral tests indexing working memory, long term memory, intelligence

Self-reported clinical symptomatology



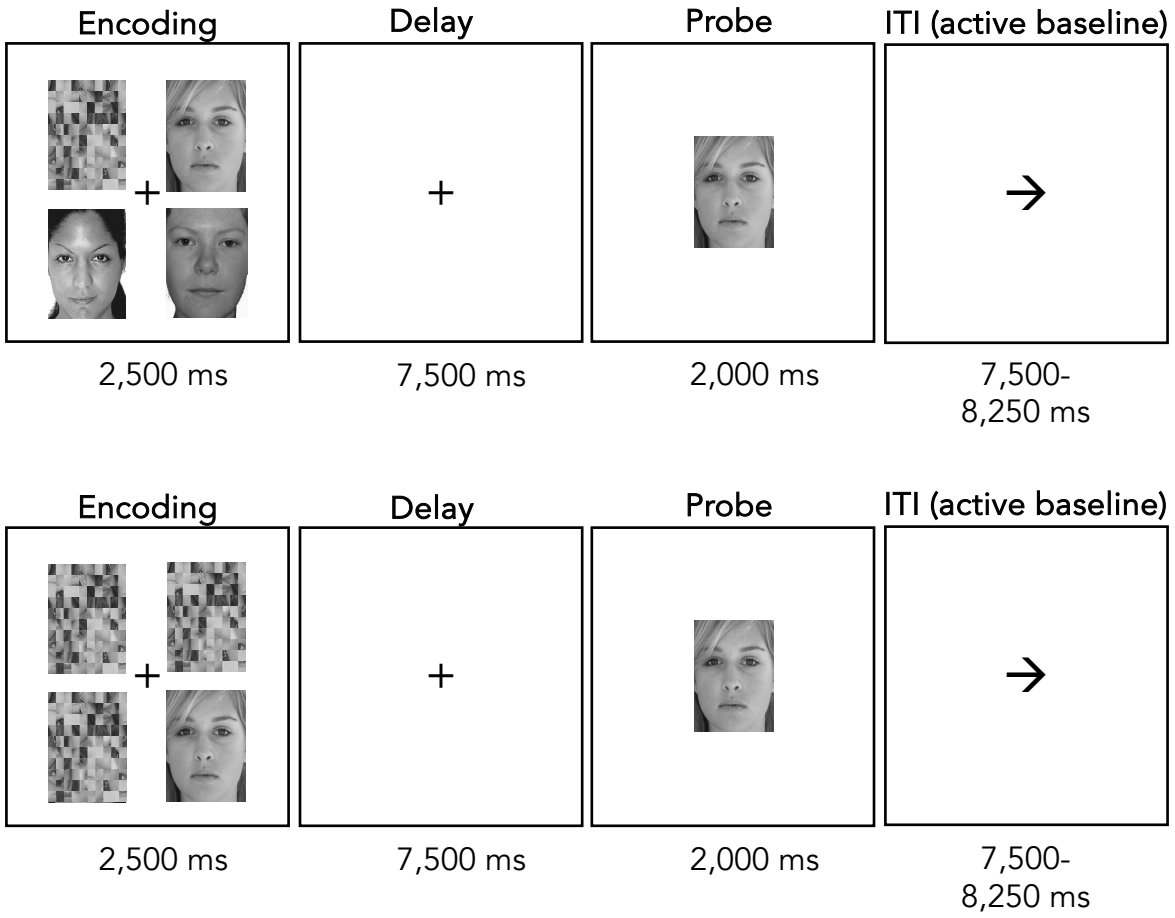
Resting state fMRI, Delayed Face Recognition task, Structural MRI

→ All data available on NIMH Data Archive (Multi-Level Assays of Working Memory and Psychopathology)

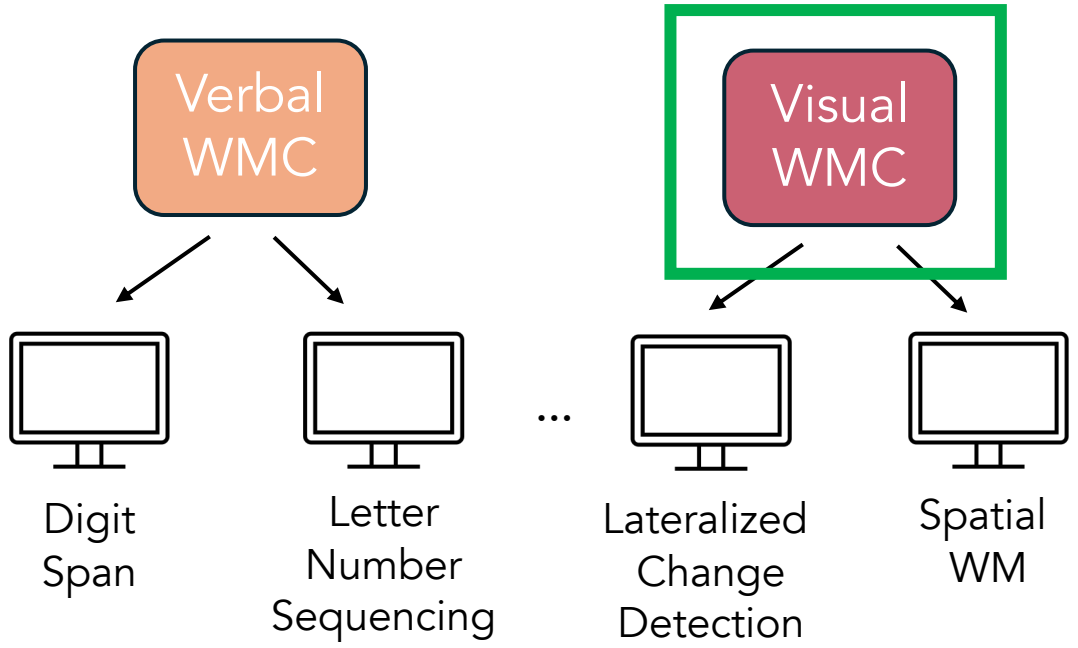
Data collected on a either 3.0T Siemens Trio (n=72) or 3.0T Siemens Prisma (n=97) with a 32-channel head coil; TR=1.5s, TE = 34.2ms, multiband acceleration factor = 4, flip angle = 80, FoV = 19.2cm with 68 axial slices, voxel resolution $2mm^{3.}$ Also collected a T1-weighted MPRAGE ($1mm^3$ voxel resolution)

Behavioral measures

Delayed Face Recognition (DFR) Task Performance

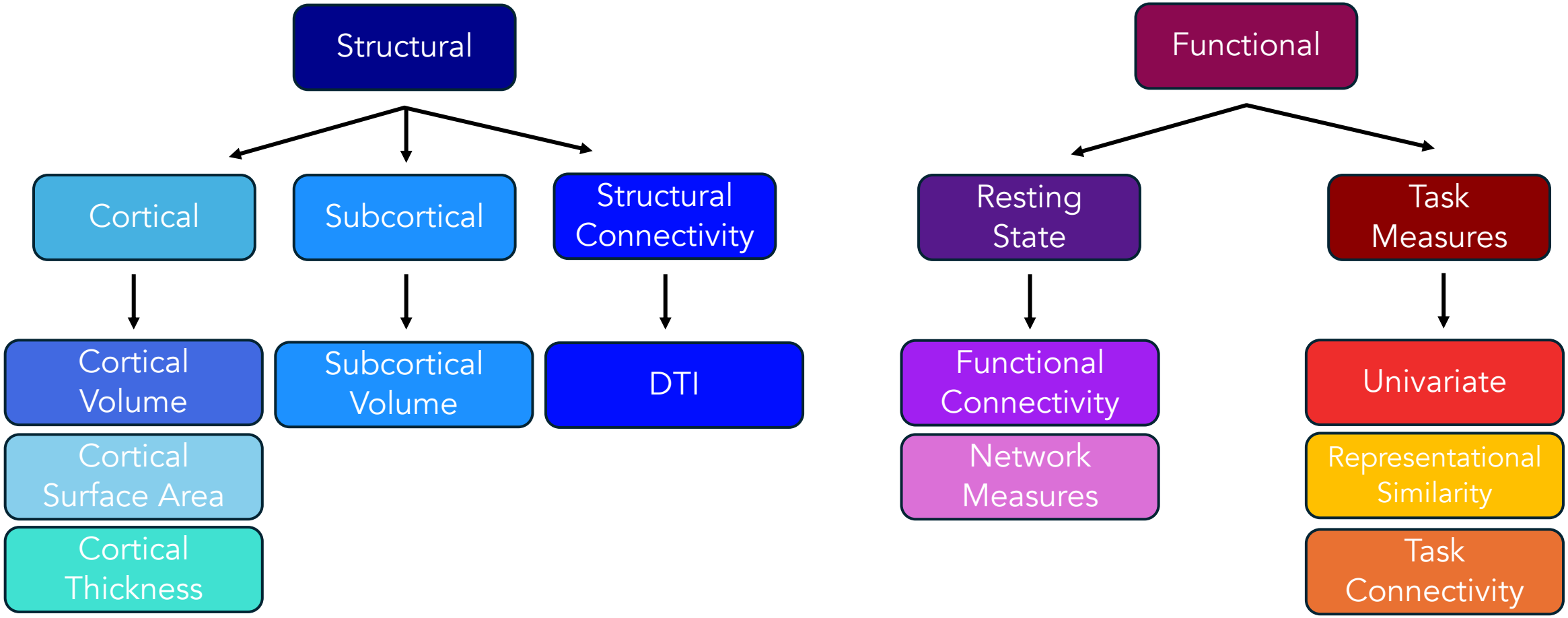


Working Memory Capacity (WMC)



World Health Organization Disability Assessment Scale 2.0 (WHODAS)

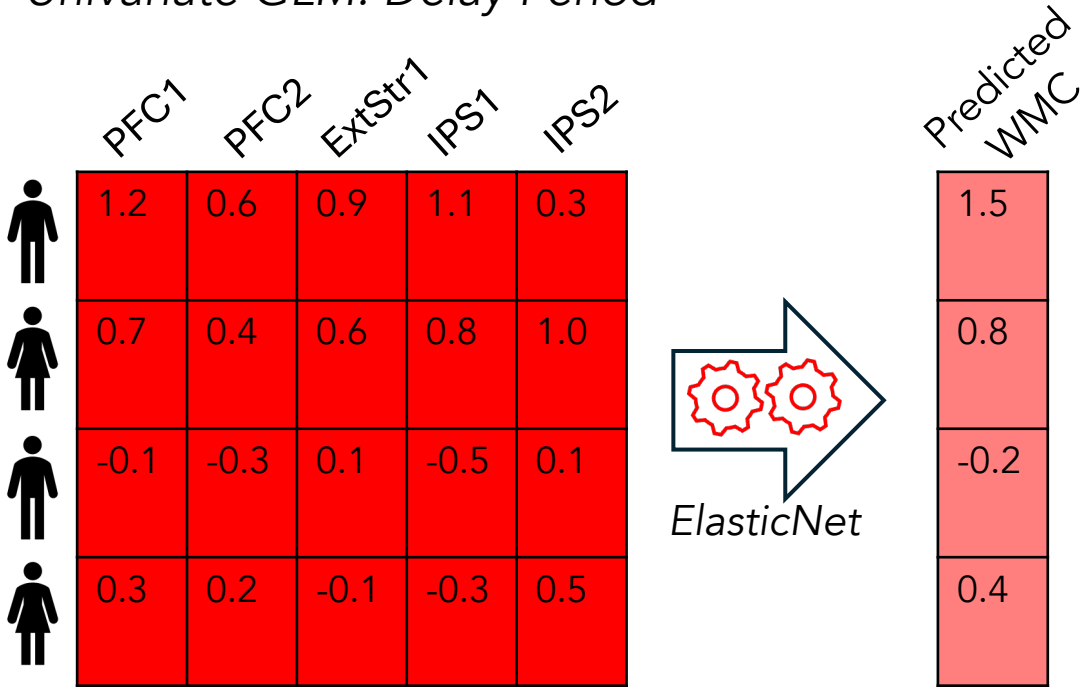
Neuroimaging Measures



Analytic framework: Stacked models

Layer 1 (ElasticNet)

Univariate GLM: Delay Period



Analytic framework: Stacked models

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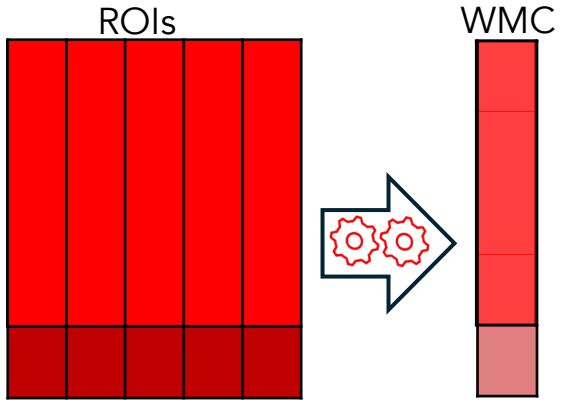
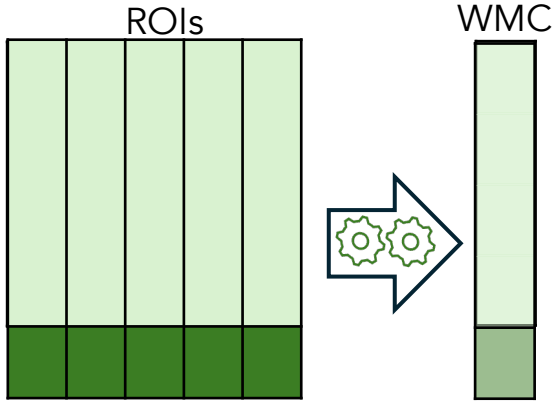
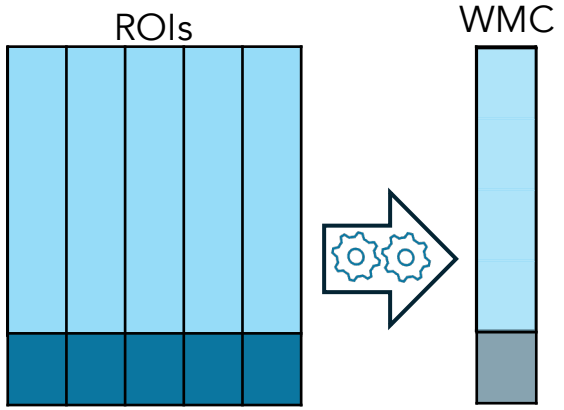
Univariate GLM: Delay Period



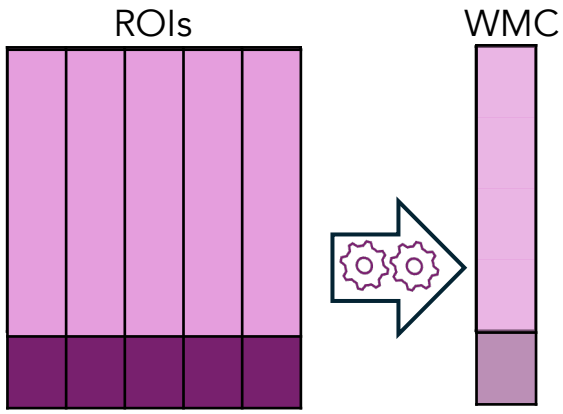
Cortical Thickness



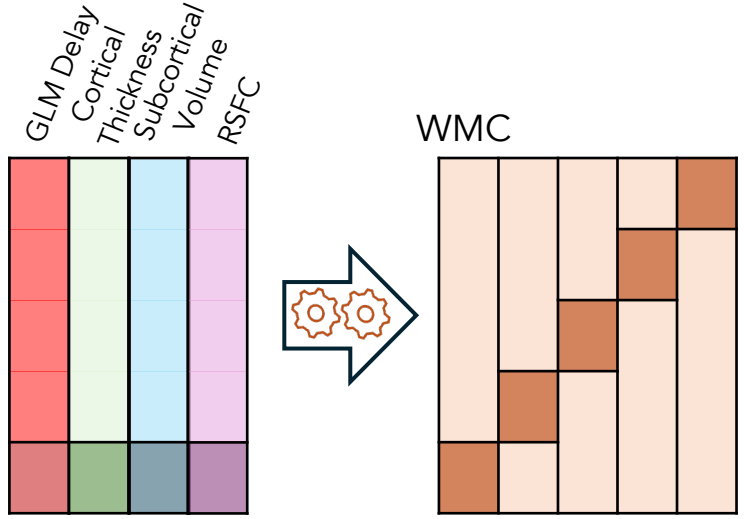
Subcortical Volume



RS Functional Connectivity



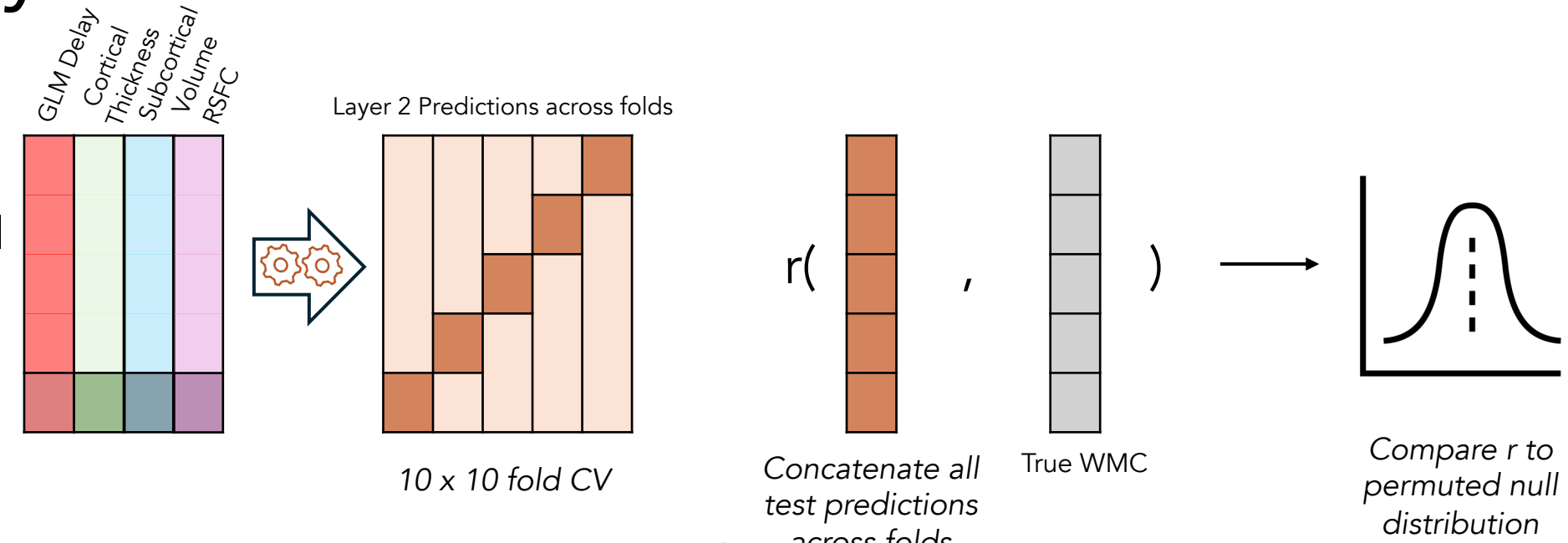
Layer 2 (LASSO)



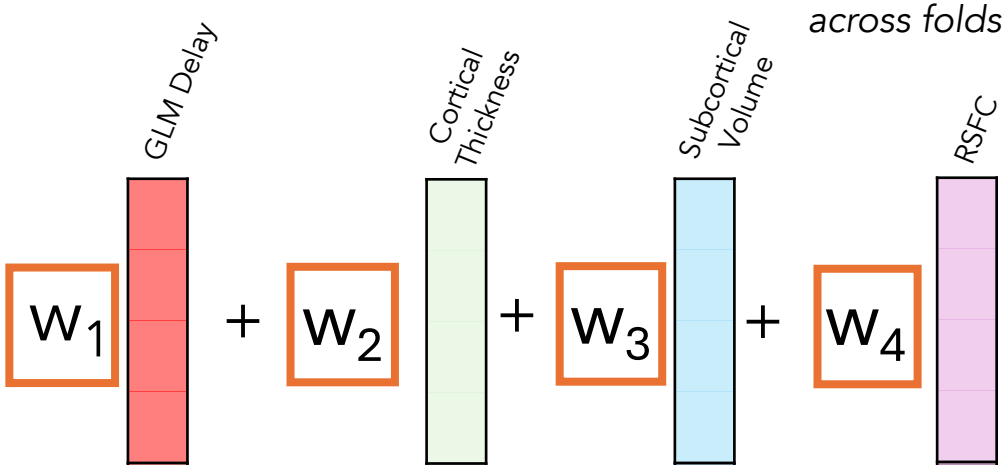
10 x 10 fold CV

Analytic framework: Stacked models

Goal 1:
Predict behavioral measures from neuroimaging measures



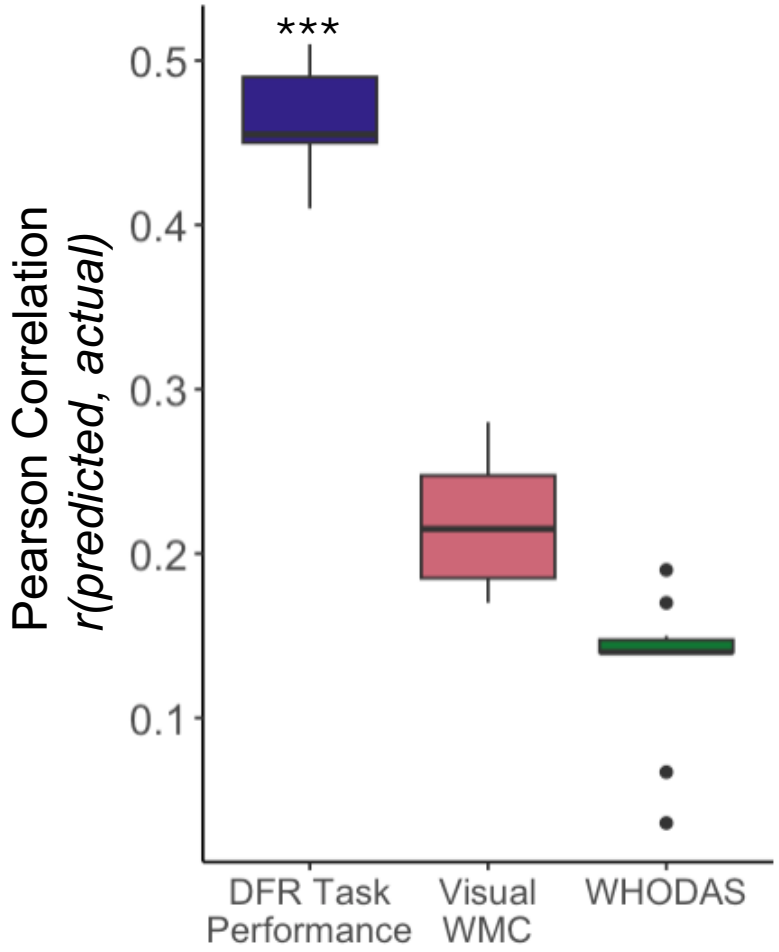
Goal 2:
Interpret the influence of each neuroimaging measure



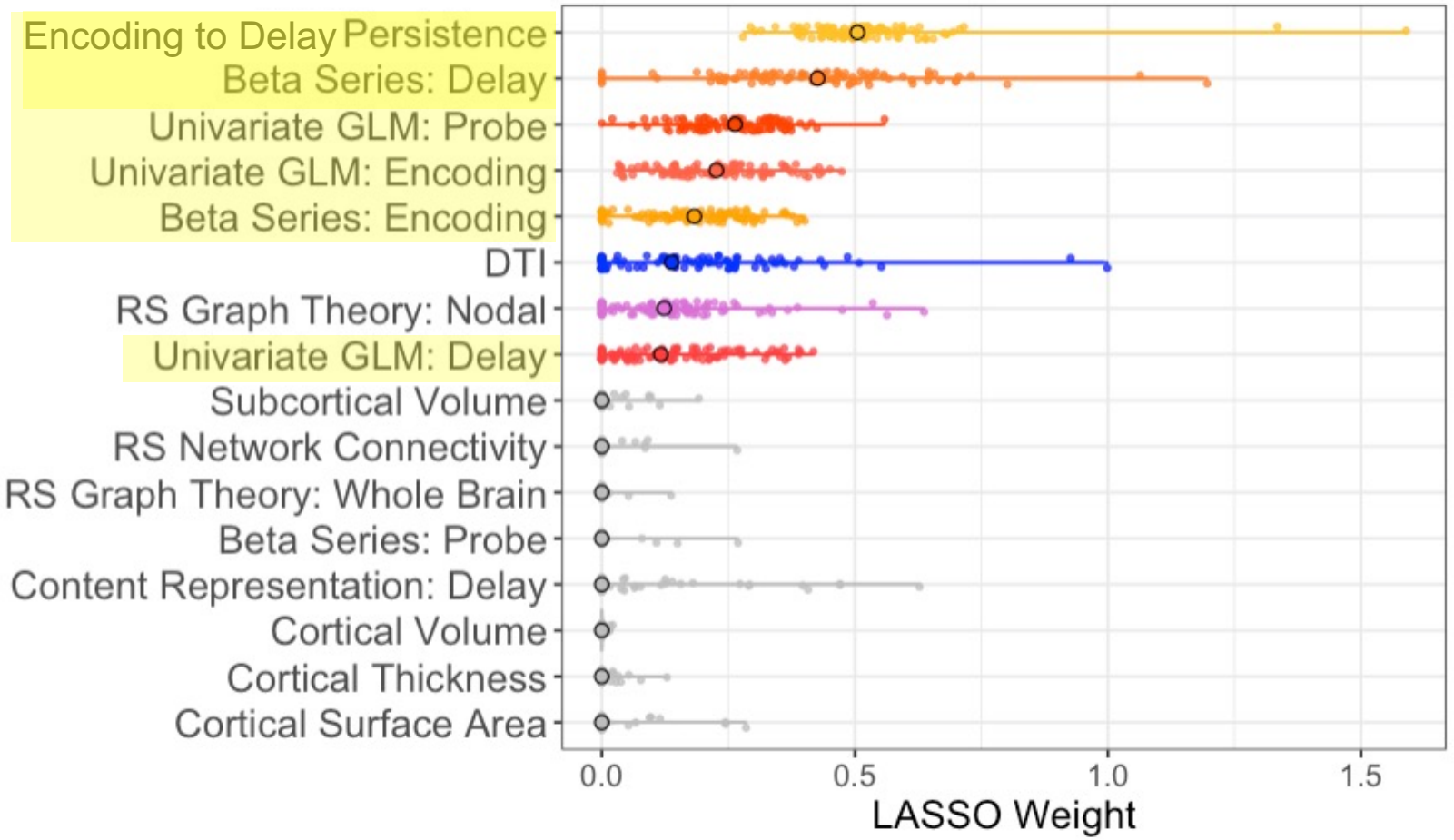
→ *Use LASSO weights as measure of influence for each neuroimaging measure on predicting a behavioral outcome*

What neuroimaging features predict individual differences in working memory capacity (WMC) and performance?

Delayed Face Recognition (DFR) Task Performance



* each dot = coefficient from one fold



Task fMRI Measures

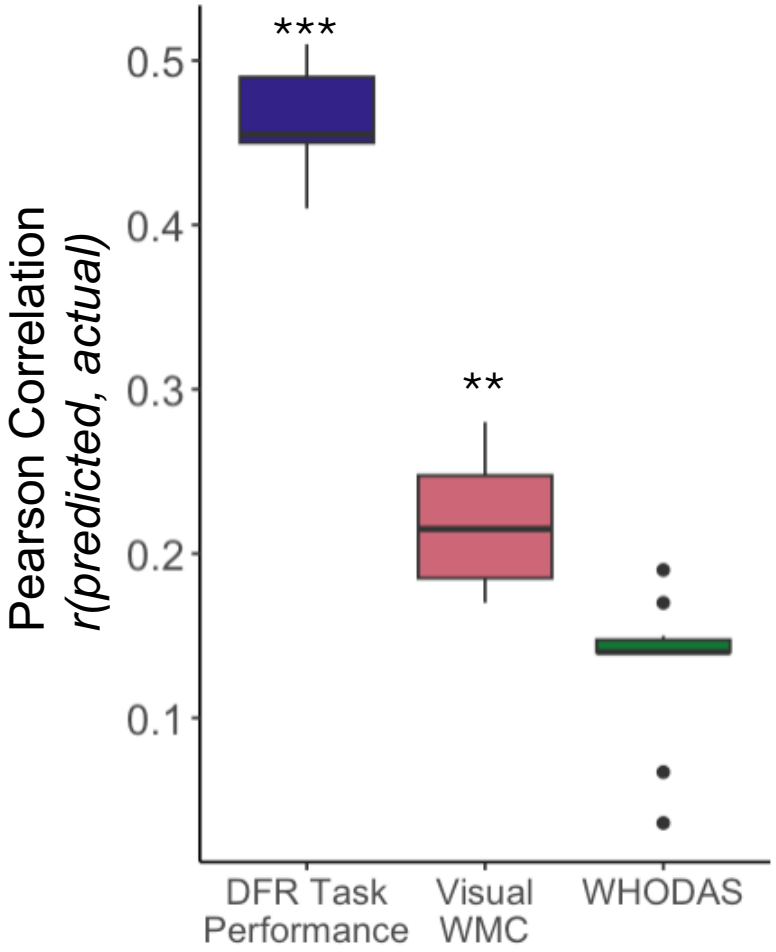
Rest fMRI Measures

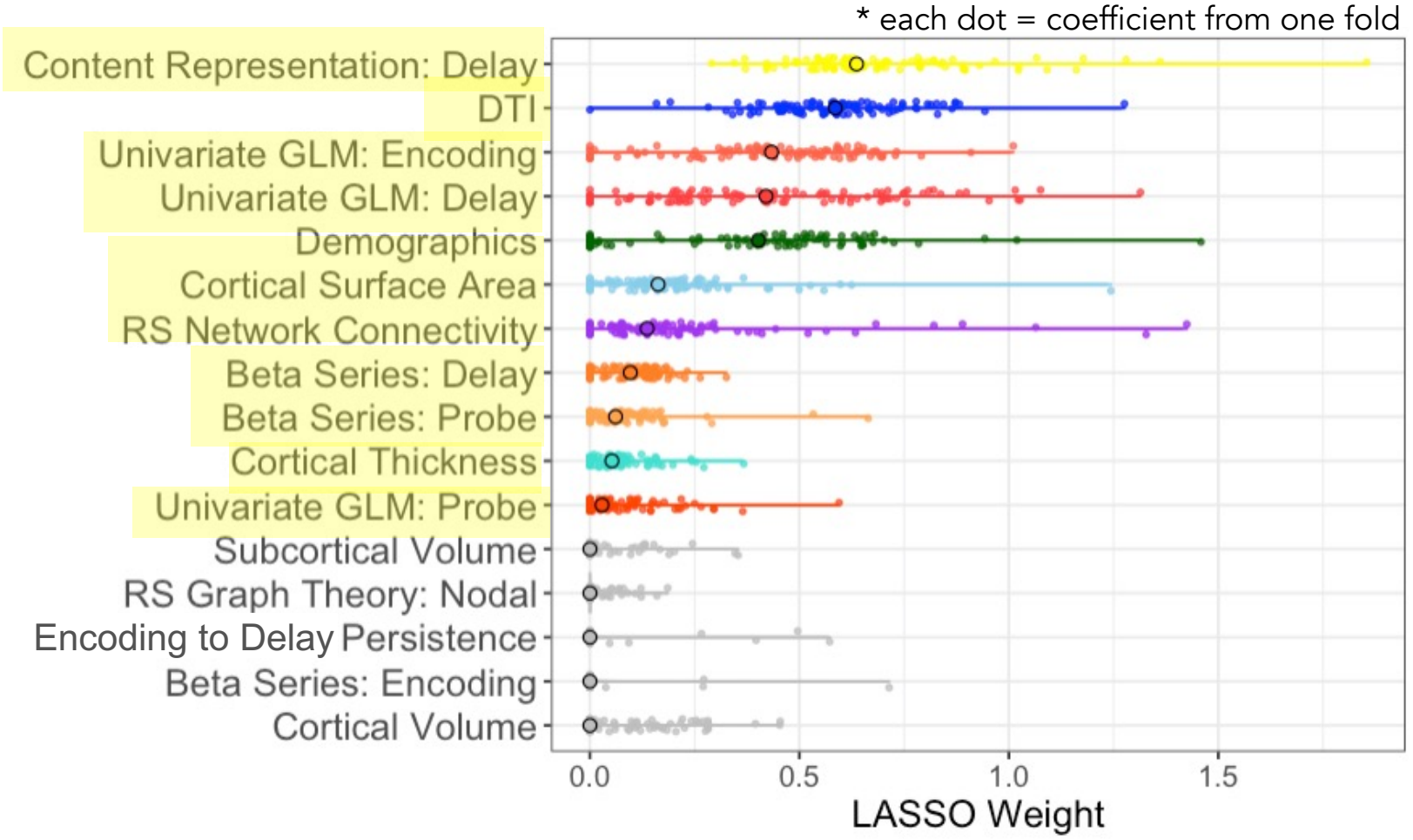
Structural MRI Measures

Non-significant (p > 0.05)

** p < 0.05, ** p < 0.01, *** p < 0.001*

Visual WMC

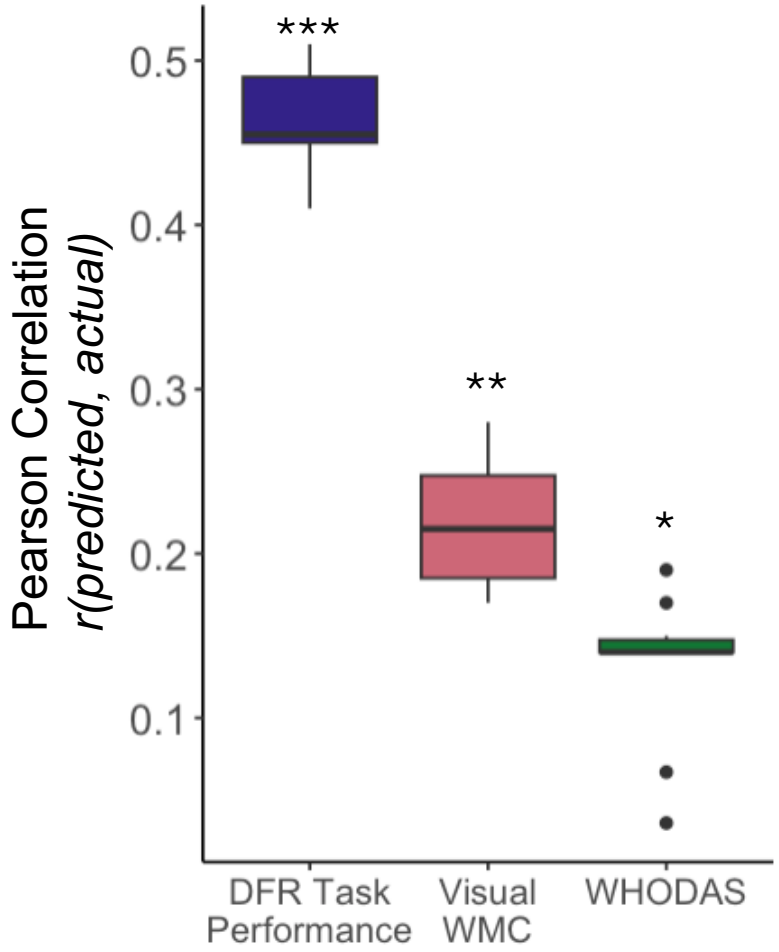


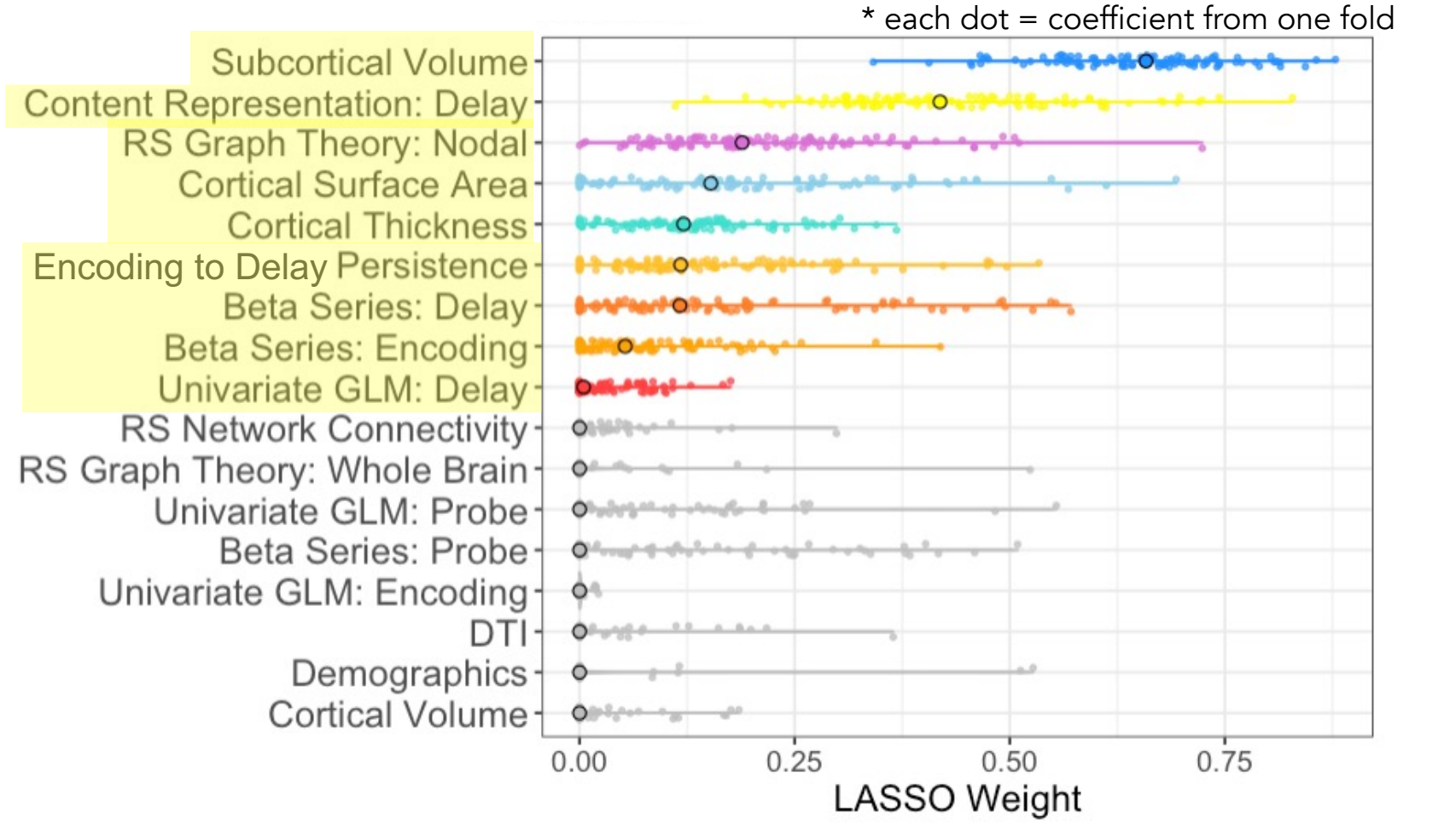


** p < 0.05, ** p < 0.01, *** p < 0.001*

Can neuroimaging features that predict individual differences in WMC *also* predict transdiagnostic psychiatric disability?

WHODAS





** p < 0.05, ** p < 0.01, *** p < 0.001*

Takeaways

- Stacked models can leverage a variety of structural and functional neuroimaging to predict individual differences in working memory performance and trait WMC
  - Diverse measures taken from scanned working memory tasks are important for predicting individual differences in working memory – not just delay period univariate GLM contrasts
  - Despite a strong correlation between WMC and task performance, distinct patterns of modalities predicted the two outcome measures
- Measures derived from a scanned working memory task are retained in models predicting indices of psychiatric disability, suggesting their potential utility as clinical biomarkers
  - Future work will examine predictive ability for specific psychiatric symptom classes

Acknowledgements

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- Catherine Sugar
- Carrie Bearden
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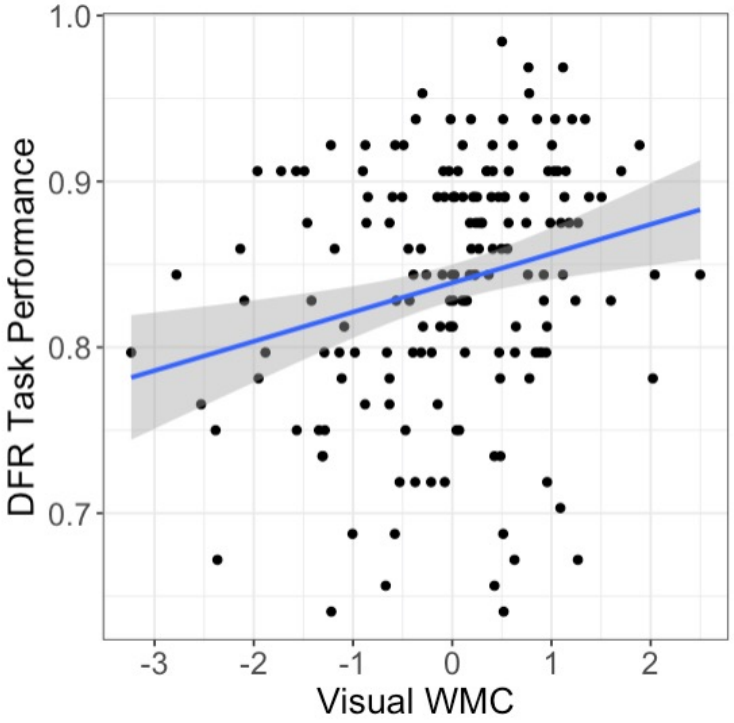
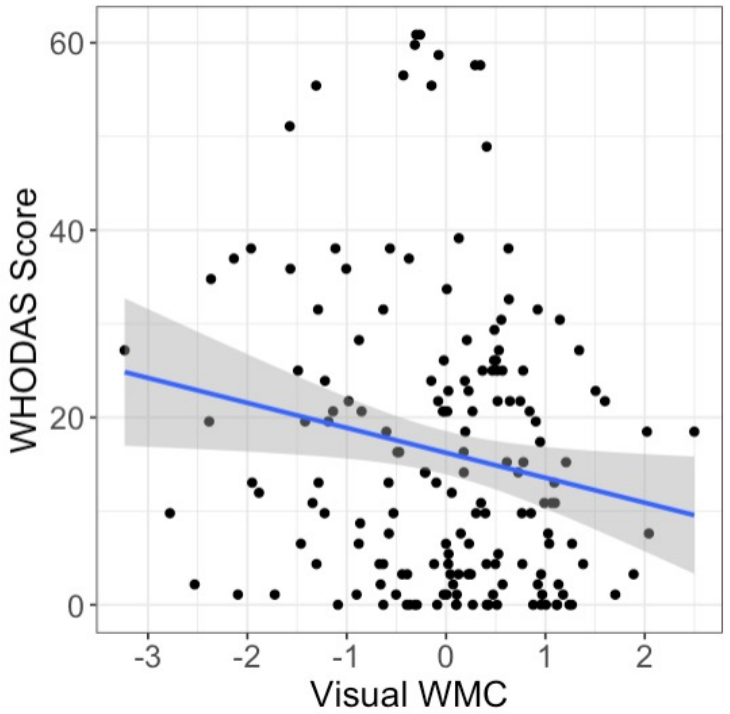
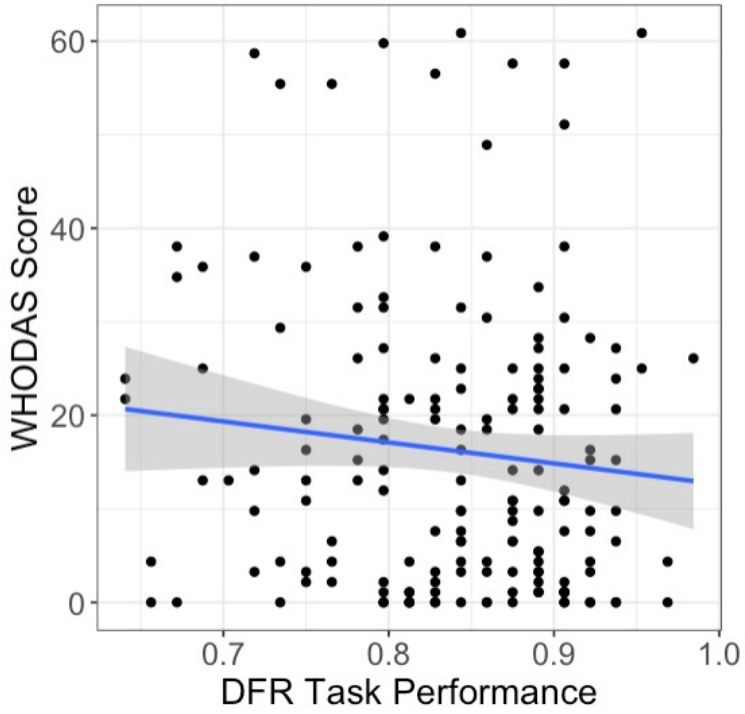
Correlation between DFR Task Performance, Visual WMC and WHODAS







$r_{(167)} = 0.24$, p = 0.002 [0.088, 0.374]

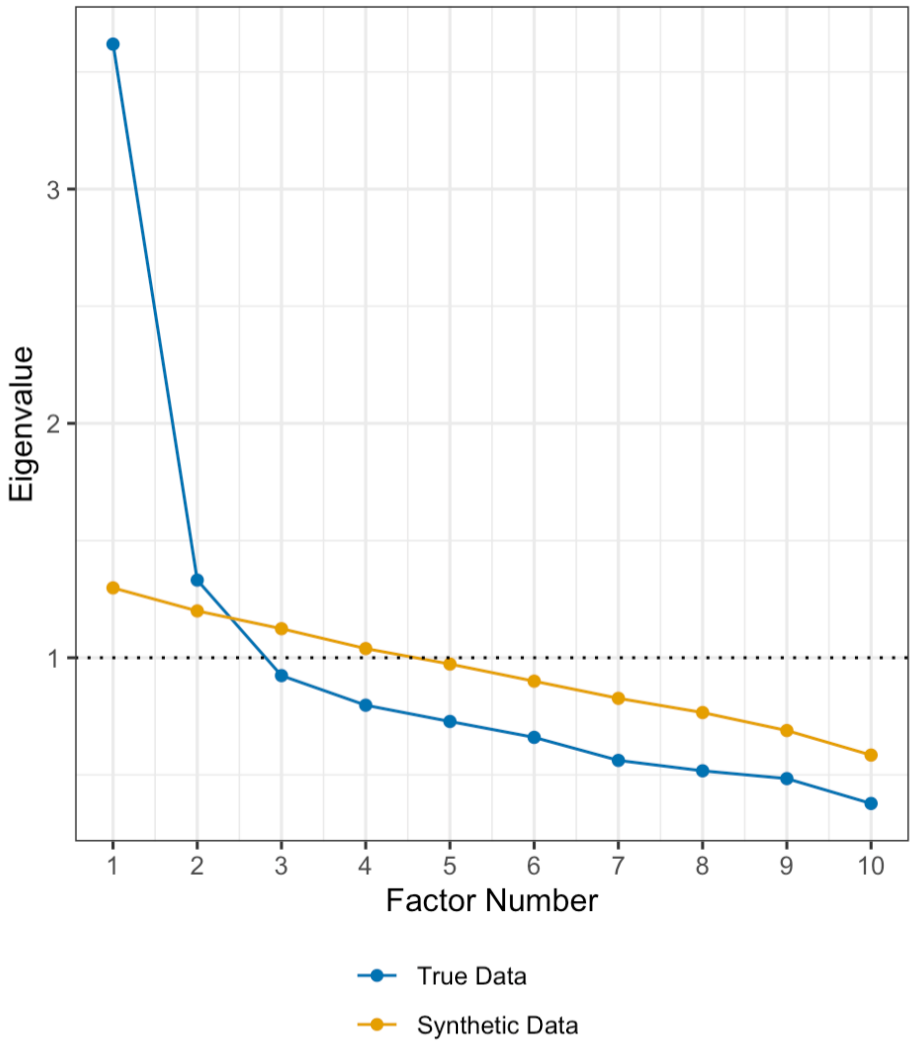
$r_{(167)} = -0.17$, p = 0.025 [-0.31, -0.02]

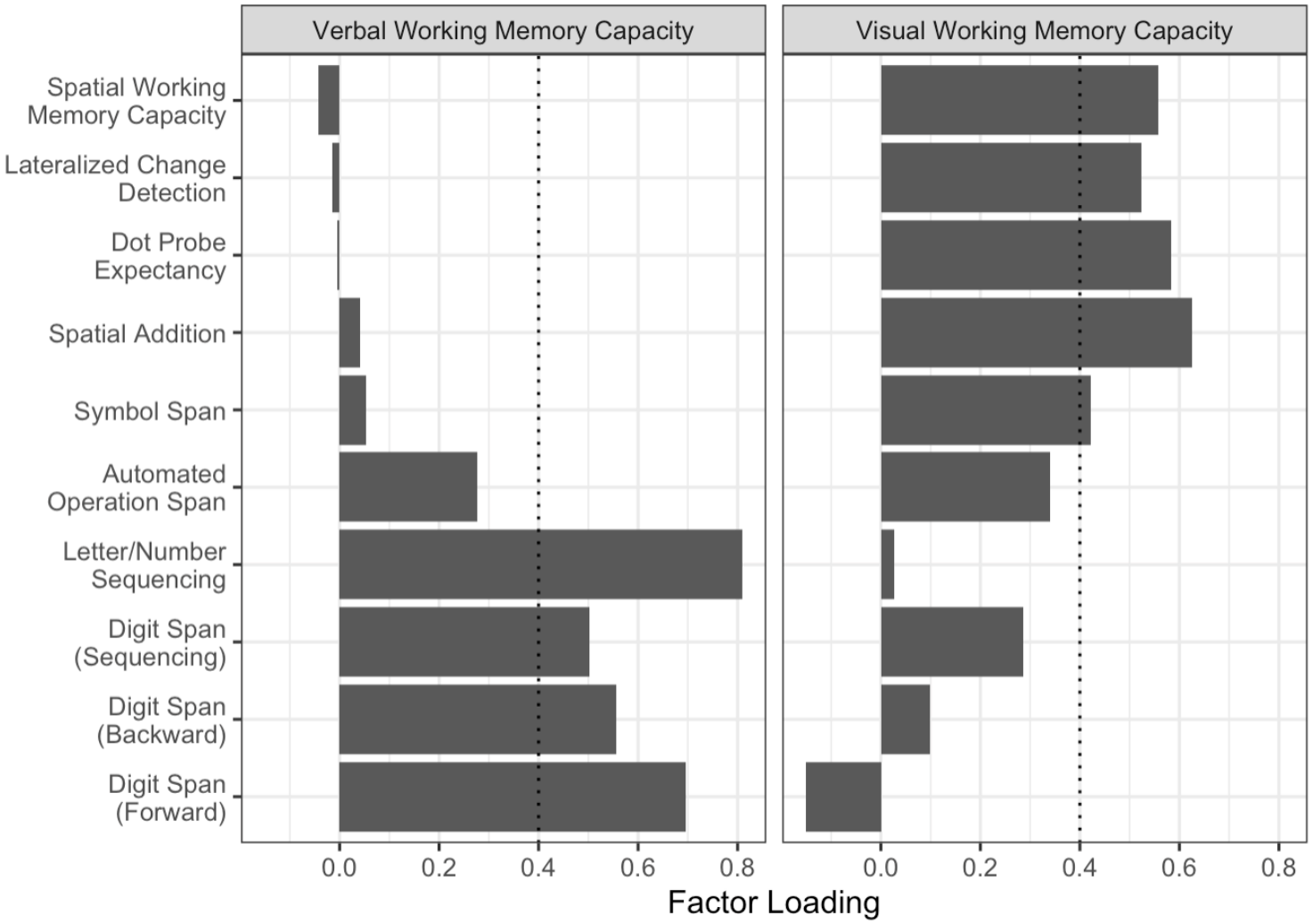
$r_{(167)} = -0.11$, p = 0.161 [-0.25, 0.043]

Behavioral Tasks

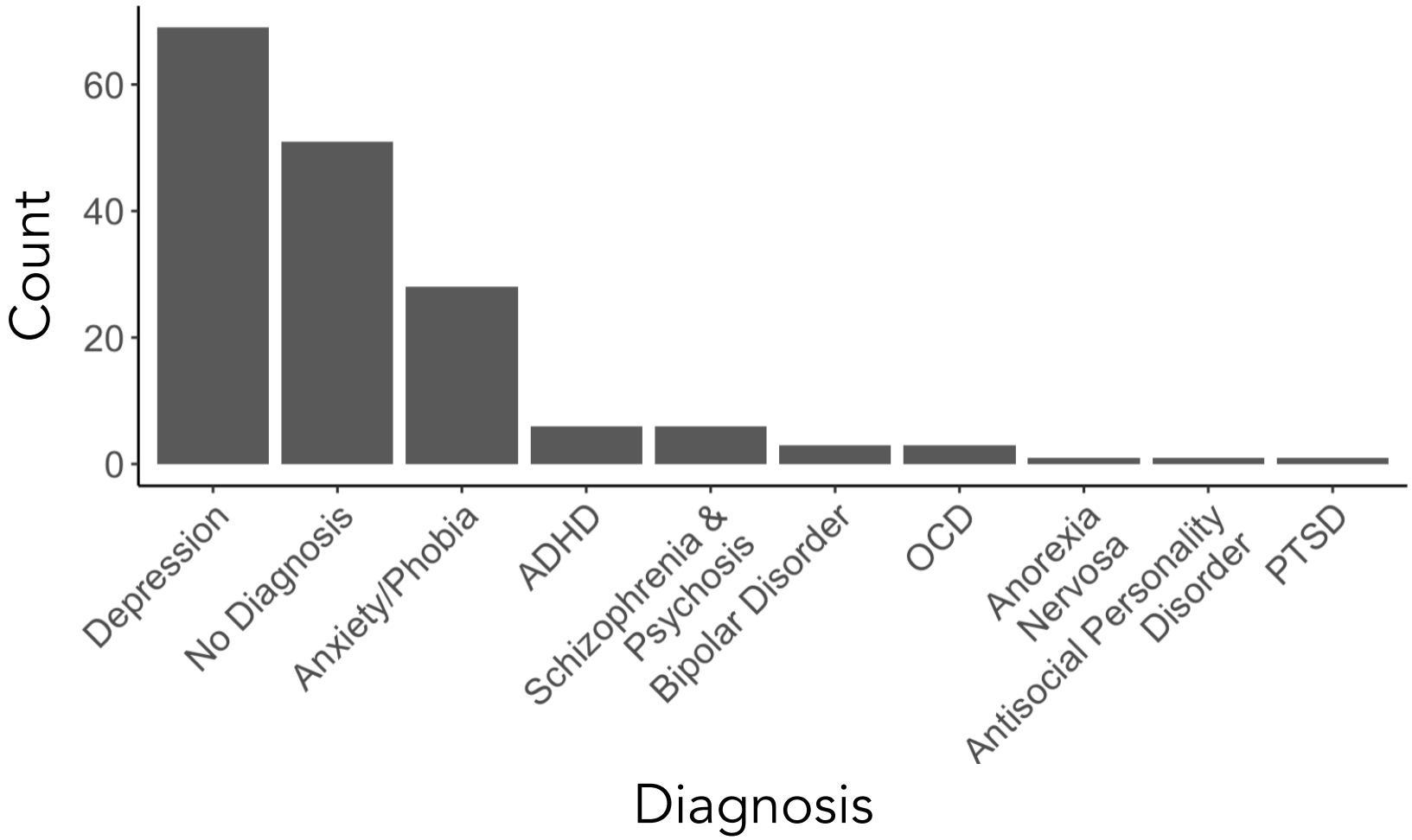
Digits Forward	Recall numbers in same order presented
Digits Backwards	Recall numbers in reverse order presented
Digit Sequencing	Recall sequence of numbers in ascending order
Letter/Number Sequencing	Recall sequence of letters and numbers with numbers in ascending order and letters in alphabetical order
Symbol Span	Recall symbols in same order presented
Spatial Addition	Add or subtract location of two grids of blue or red circles based on a set of rules
Lateralized Change Detection	Maintain color-location bindings of up to 5 colored objects (circles or lines)
Spatial Capacity	Maintain locations of up to 7 dots
Operation Span	Recall a set of letters in order while solving math problems in between each successive letter

EFA

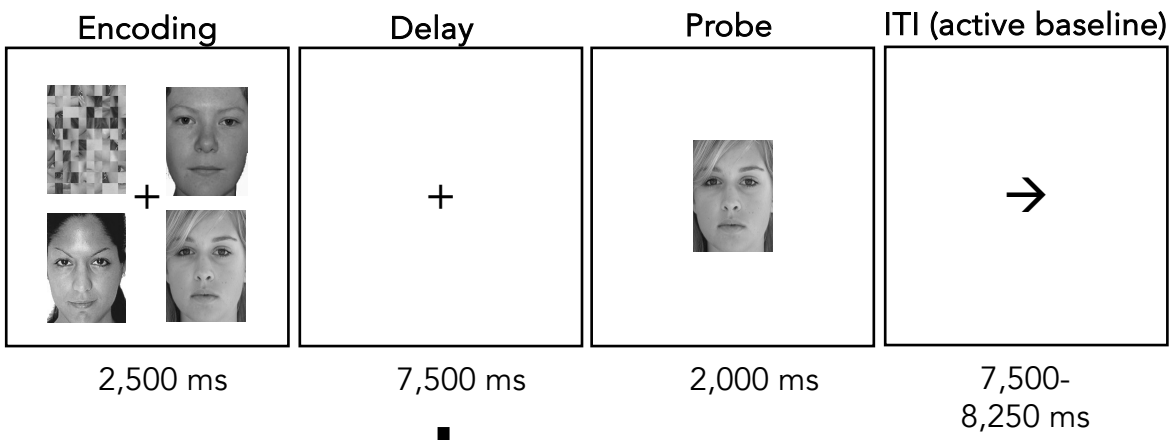

Eigenvalue
3
2
1
1
2
3
4
5
6
7
8
9
10
Factor Number
True Data
Synthetic Data

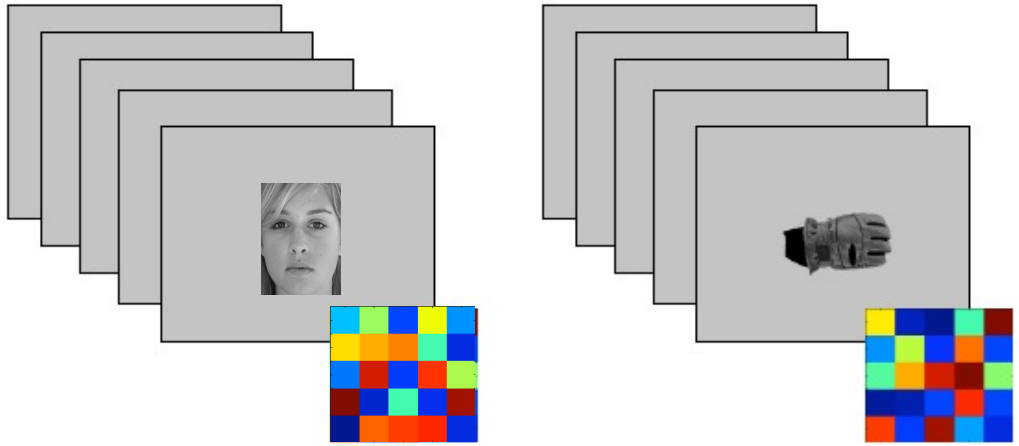

Verbal Working Memory Capacity
Visual Working Memory Capacity
Spatial Working Memory Capacity
Lateralized Change Detection
Dot Probe Expectancy
Spatial Addition
Symbol Span
Automated Operation Span
Letter/Number Sequencing
Digit Span (Sequencing)
Digit Span (Backward)
Digit Span (Forward)
0.0
0.2
0.4
0.6
0.8
Factor Loading

Distribution of diagnoses in sample



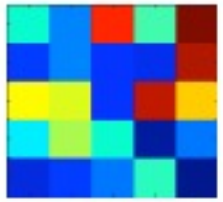
Feature modalities: Content representation during delay



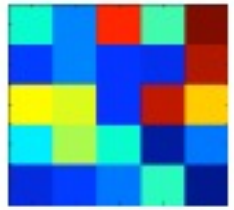
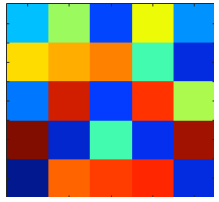
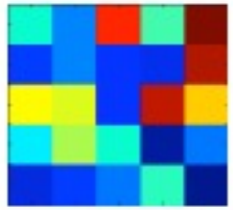
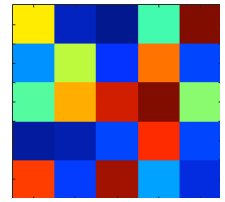


Face template

Object template



Delay period multivariate pattern

r( , ) - r( , )

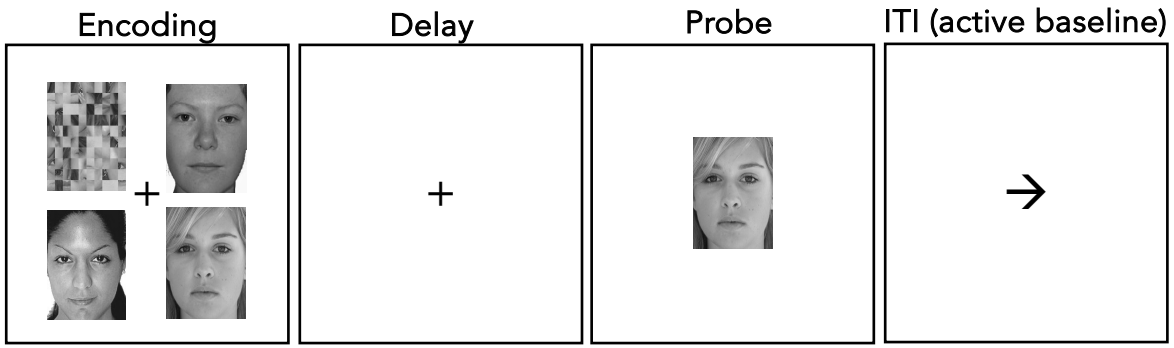
Delay period multivariate pattern

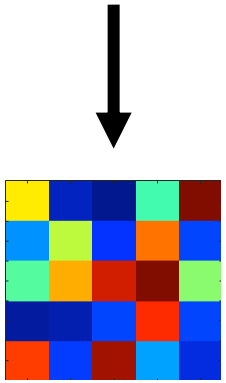
Face template

Delay period multivariate pattern

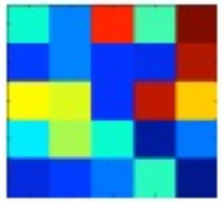
Object template

Feature modalities: Encoding-to-delay persistence

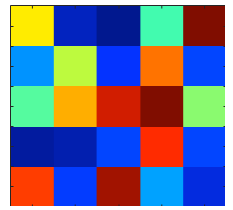
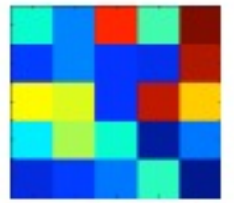




Encoding period multivariate pattern



Delay period multivariate pattern

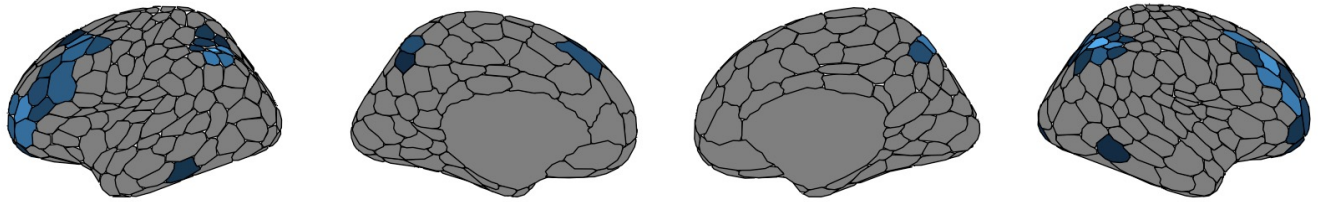
r( , )

Encoding period multivariate pattern

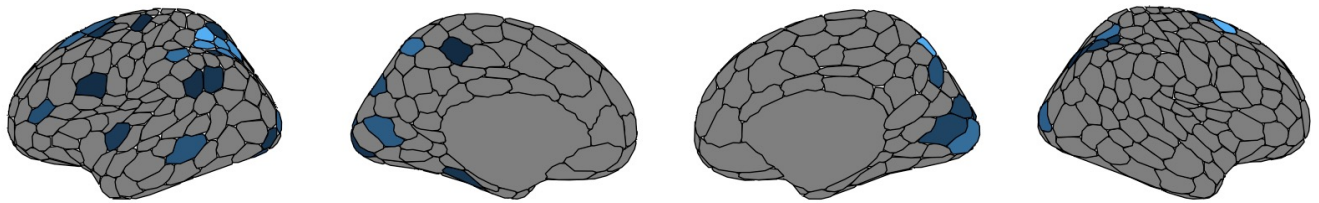
Delay period multivariate pattern

Task fMRI load effects

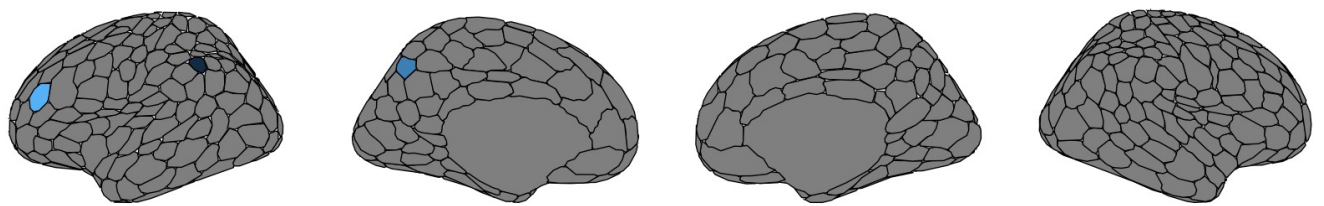
Univariate GLM (Delay)



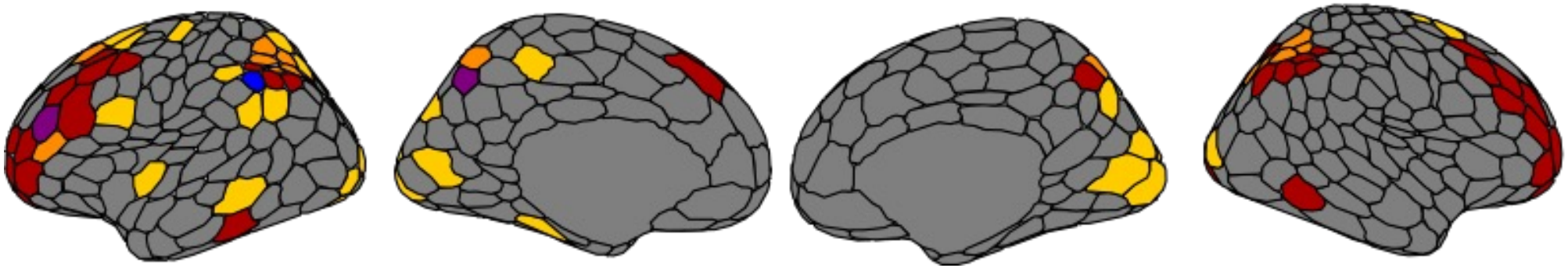
Maintenance of Content (Delay)



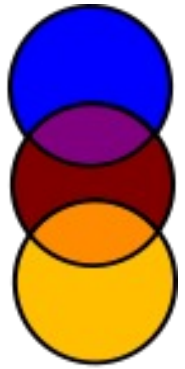
Encoding to Delay Pattern Stability



Feature Space



84 regions across Control (37), Visual (15), Dorsal Attention (14), Default (9), Salience/Ventral Attention (8) and Somato-Motor (1) showed **high > low load effects** in any task fMRI measure

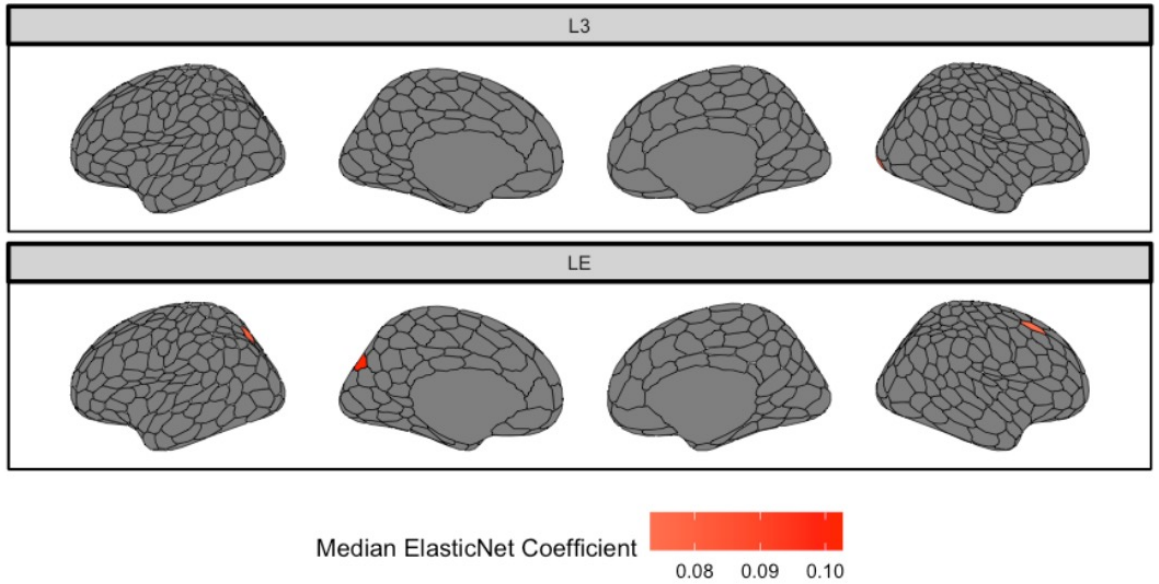


Representational Persistence

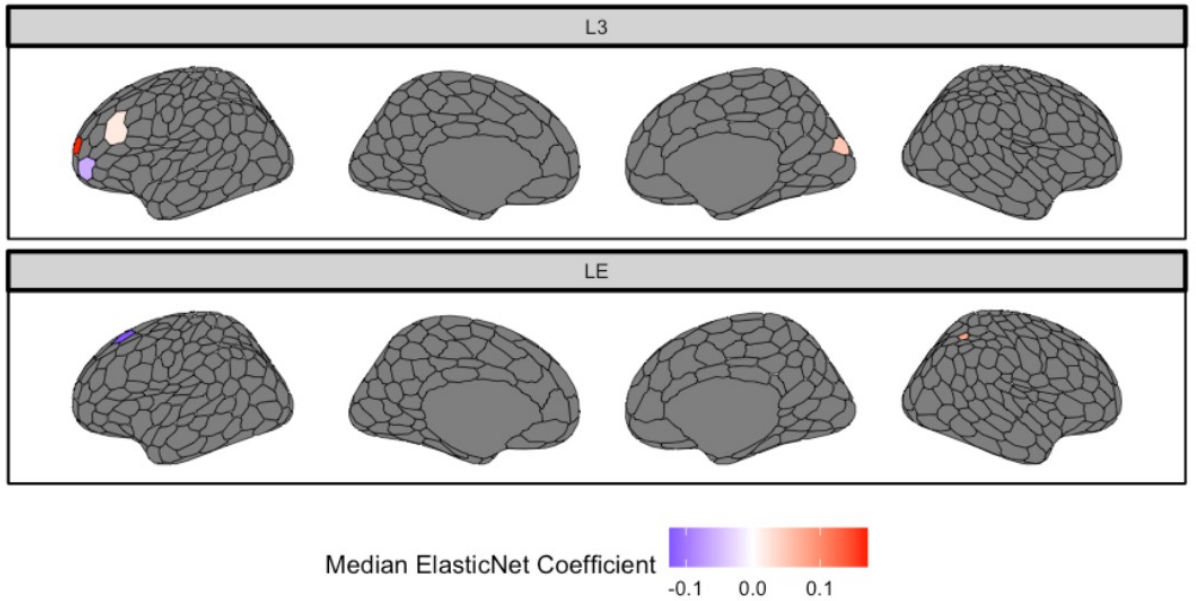
Univariate GLM: Delay

Content Representation: Delay

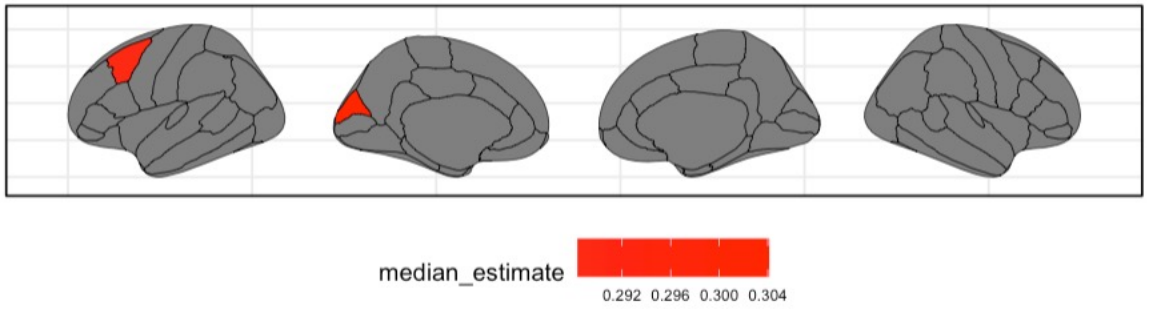
Visual WM - FSRC



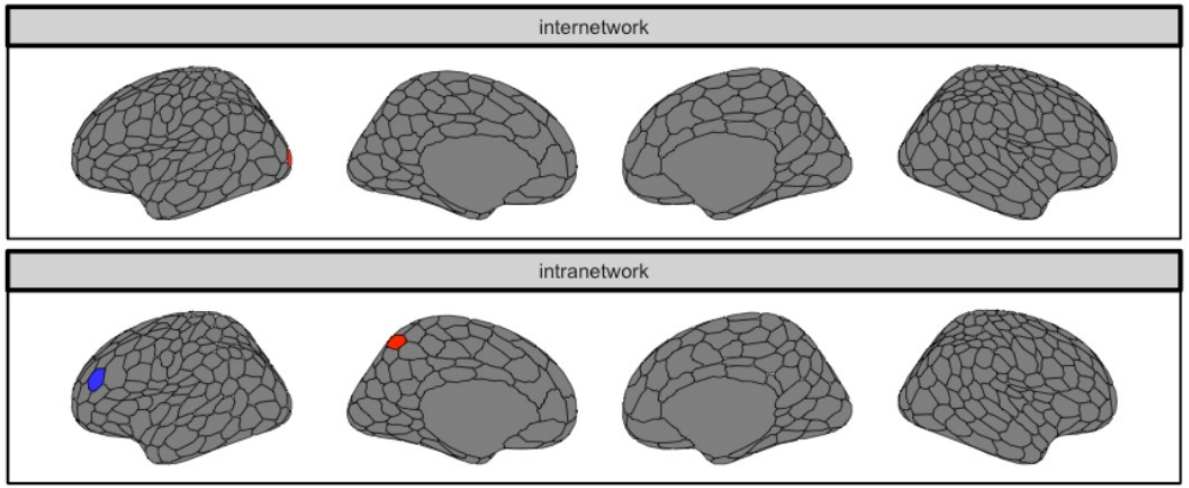
Visual WM - encoding_univ



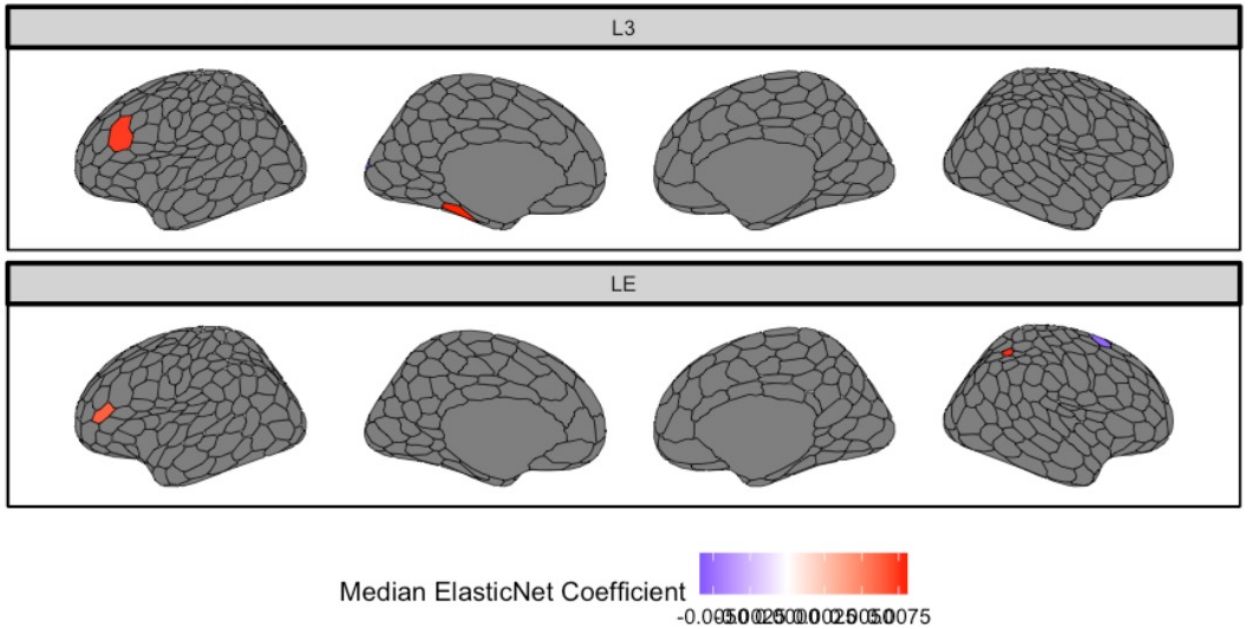
Visual WM - cortical_surface_area



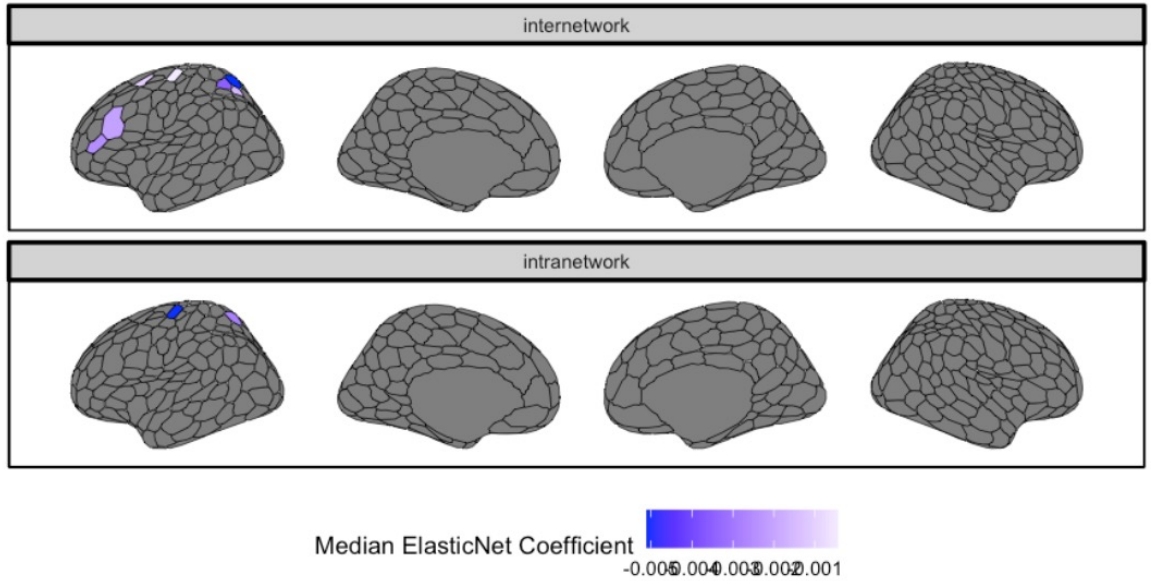
Visual WM - RS_network_conn_wide



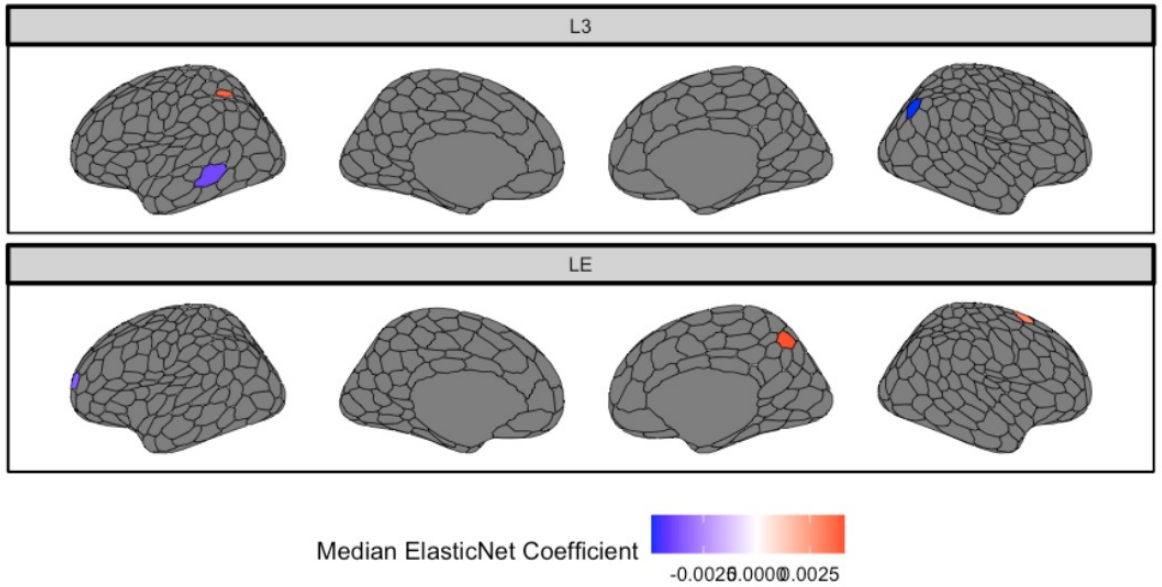
DFR - encoding_to_delay



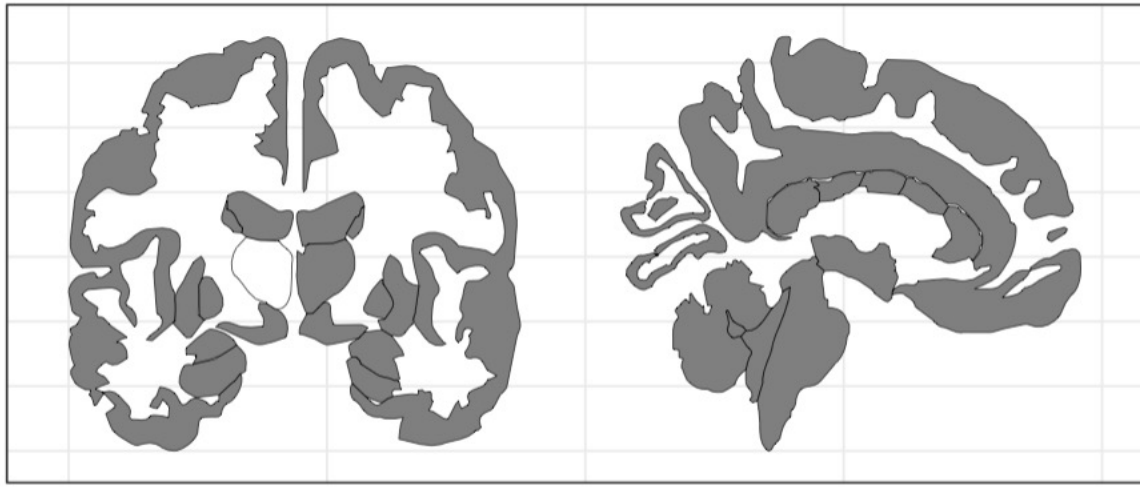
DFR - delay_beta_series



DFR - encoding_univ



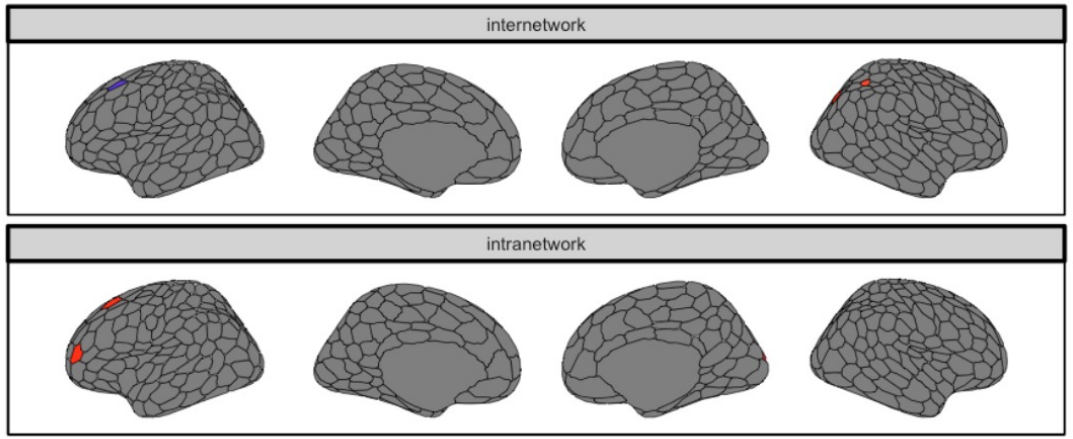
WHODAS - subcortical_volume



median_estimate

-3.529625

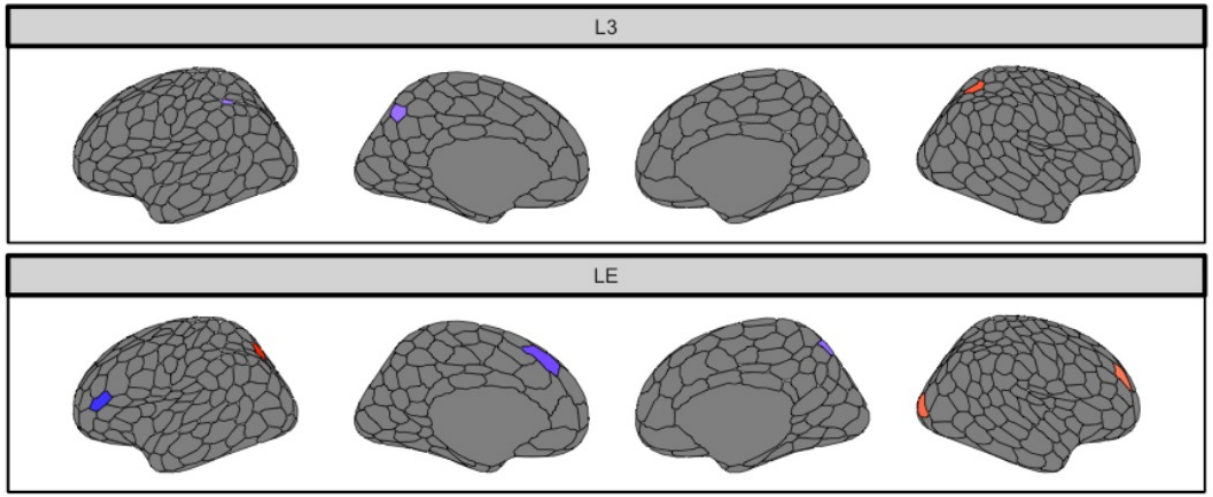
WHODAS - cue_beta_series



Median ElasticNet Coefficient

-2 0 2 4

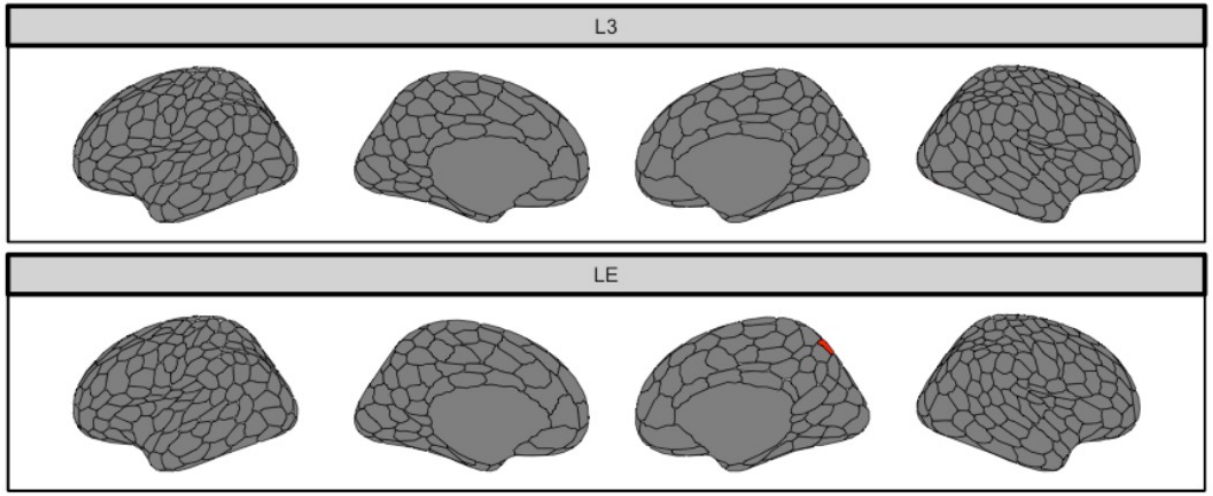
WHODAS - FSRC



Median ElasticNet Coefficient

-2 -1 0 1 2

WHODAS - encoding_to_delay



Median ElasticNet Coefficient

3.40 3.45 3.50 3.55 3.60 3.65

Stacked vs Flat Models