Assessing the cross-cohort generalizability of connectivity-based fluid cognition prediction pattern

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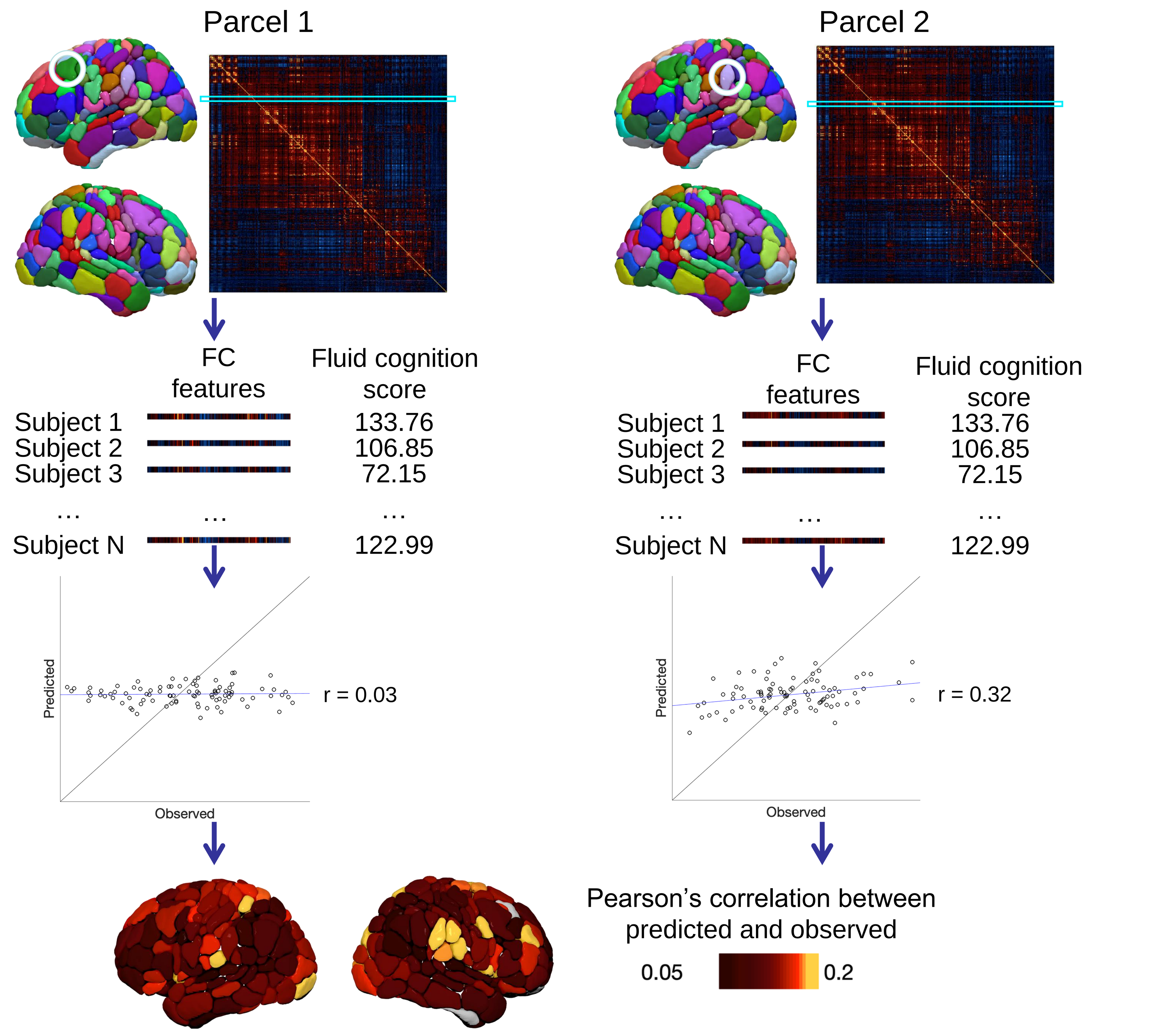
Introduction

- An increasing number of studies are investigating brain-behavior relationships using connectivity-based psychometric prediction (CBPP) in openly available datasets.
- The cross-cohort replicability of the derived brain-behavior association remains an open challenge.
- To assess the replicability of brain-behavior associations patterns, we used a previously developed region-wise CBPP approach [1], representing brain-behavior association by the pattern of parcel-specific prediction accuracies variation across the brain.
- Furthermore, we assessed the cross-cohort generalizability of prediction models, where models trained in one cohort is applied to a completely new cohort

Region-wise CBPP



Data & Preprocessing

- We selected 4 cohorts with distinct imaging protocols, psychometric tests, and age range.

	HCP-YA [2]	HCP-A [3]	eNKI-RS [4]	GSP [5]
Number of subjects (N)	931	601	970	867
Age	28.81±3.70	58.11±13.88	39.70±23.15	21.59±2.84
Length of resting-state runs	14.4 min / 1200 frames	488 frames	10 min / 900 frames	120 frames
Repetition time (TR)	720 ms	720 ms	645 ms	3000 ms
Resolution of resting-state scans	2mm isotropic	2mm isotropic	3mm isotropic	3mm isotropic
Fluid cognition measures	fluid cognition composite score	fluid cognition composite score	Wechsler Abbreviated Scale of Intelligence	Shipley IQ
Confounding variables	sex, age, age^2, sex*age, sex*age^2, handedness, brain size, intracranial volume, acquisition quarter	sex, age, age^2, sex*age, sex*age^2, handedness, brain size, intracranial volume		
Preprocessing	HCP Minimal Processing Pipelines, ICA-FIX	HCP Minimal Processing Pipelines, ICA-FIX	fMRIPrep (default parameter, including ICA-AROMA)	Fieldmap correction, motion correction, slice-time correction, spatial normalization, ICA-FIX
	Nuisance regression (WM, CSF, 24 motion parameters)			
Parcellation	300-parcel Schaefer cortical atlas [6] + 50-parcel Melbourne subcortex atlas [7]			
Functional connectivity	Pearson correlation			

References: [1] Wu J, et al. 2021. "A connectivity-based psychometric prediction framework for brain-behavior relationship studies". *Cerebral Cortex*. [2] Van Essen DC, et al. 2012. "The Human Connectome Project: a data acquisition perspective". *Neuroimage*. [3] Bookheimer SY, et al. 2019. "The lifespan Human Connectome Project in aging: An overview". *NeuroImage*. [4] Nooner KB, et al. 2021. "The NKI-Rockland Sample: A model for accelerating the pace of discovery science in psychiatry". *Frontiers in Neuroscience*. [5] Holmes AJ, et al. 2015. "Brain Genomics Superstruct Project initial data release with structural, functional, and behavioral measure". *Scientific Data*. [6] Schaefer A, et al. 2018. Local-Global parcellation of the human cerebral cortex from intrinsic functional connectivity MRI. *Cerebral Cortex*. [7] Tian Y, et al. 2020. "Topographic organization of the human subcortex unveiled with functional connectivity gradients". *Nature Neuroscience*. [8] Cortes C and Vapnik VN. 1995. "Support-vector networks:. *Machine Learning.*

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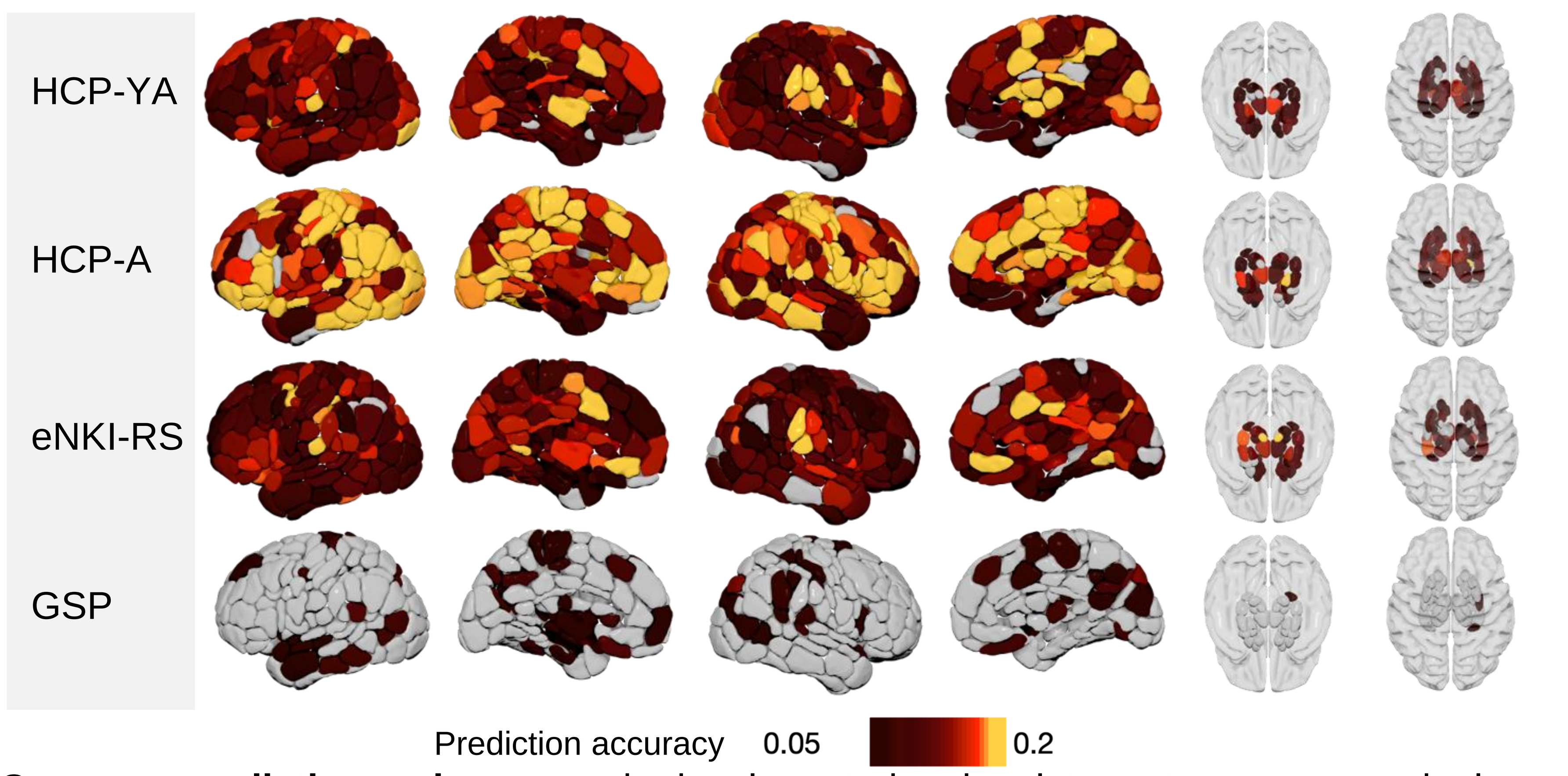
Replicability of prediction patterns

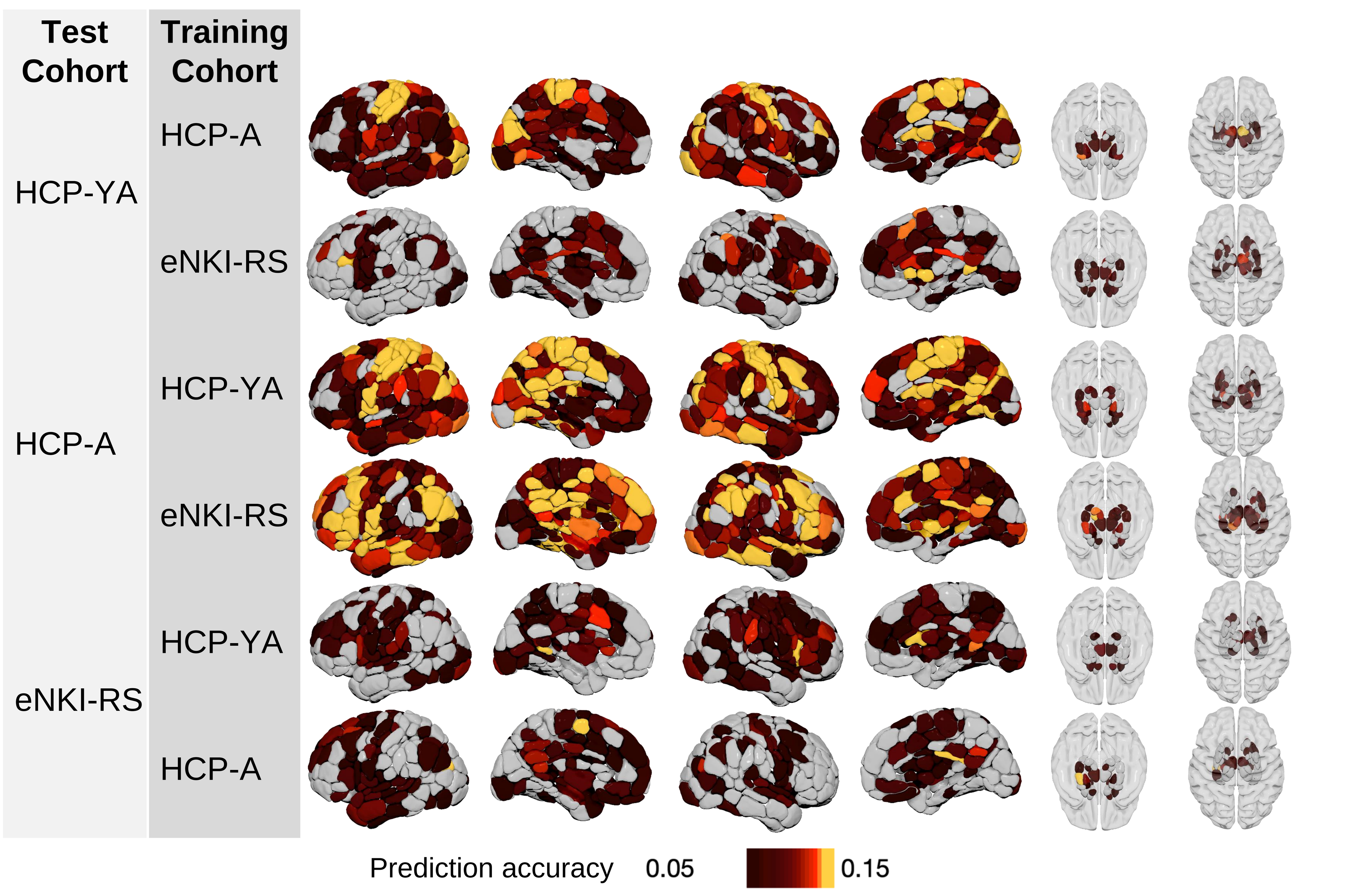
- **Prediction**: support vector regression [8] with 100 repeats of 10-fold cross-validation (family members were always kept in the same fold for HCP-YA)
- **Evaluation**: Pearson's correlation between predicted and observed values



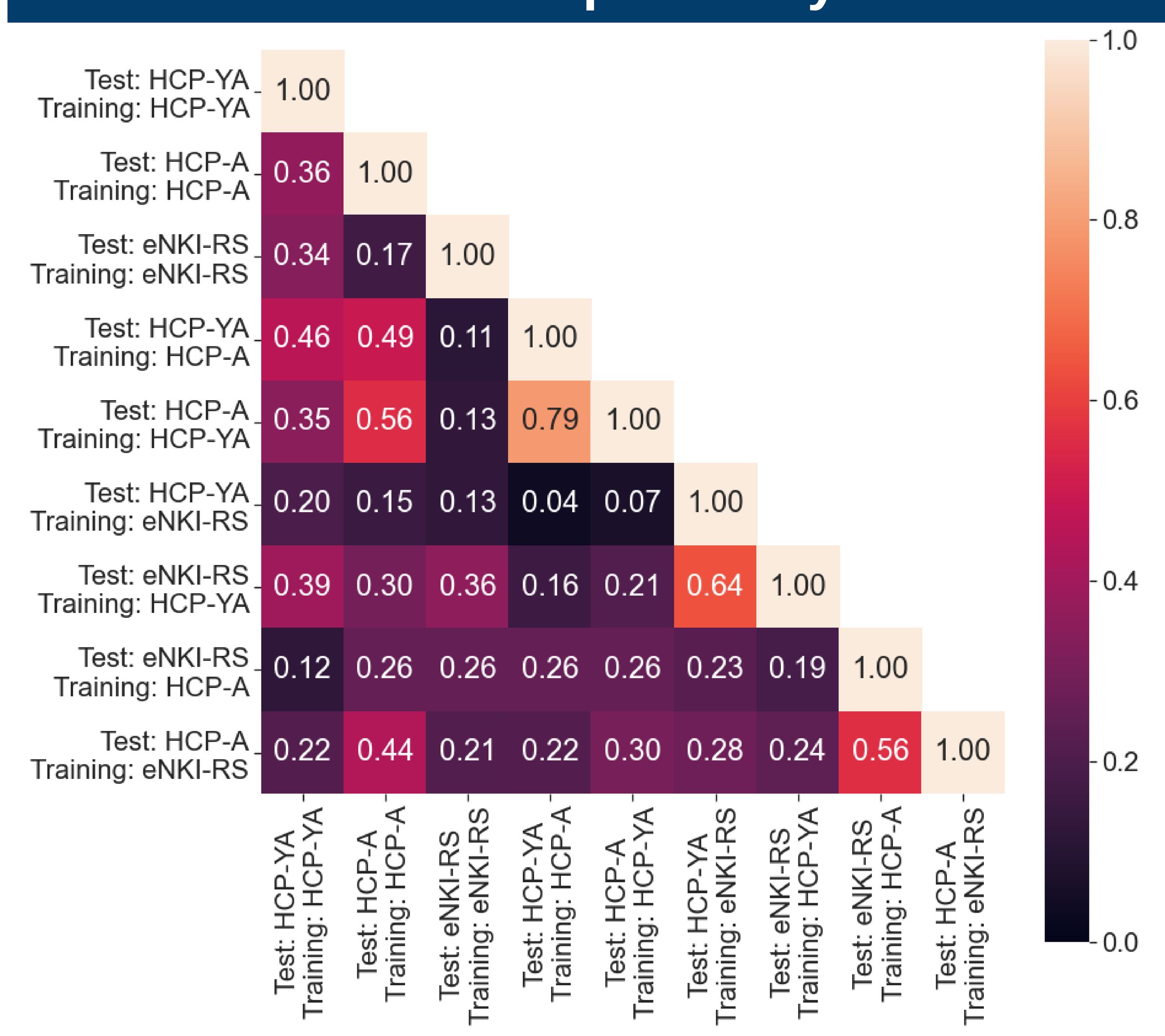
- **Common predictive regions**: anterior insula, anterior cingulate cortex, supramarginal gyrus

Generalizability of prediction models

- **Prediction**: support vector regression [8] trained in one cohort & tested on another
- **Evaluation**: Pearson's correlation between predicted and observed values



Replicability & Generalizability



- To **quantify** replicability and generalizability, we computed Pearson's correlation between each pair of prediction patterns
- The highest similarity is observed between prediction patterns using the same pair of cohorts, but swapping the training and test set

Conclusion

- We found low replicability of brain prediction patterns across the 4 cohorts.
- In HCP-YA, HCP-A and eNKI-RS, some extent of replicability can be observed, revealing a set of common brain regions potentially involved in fluid cognitive ability.
- We demonstrated generalizability to a low to moderate extent in 3 of the 4 cohorts.
- Overall, replicability of brain prediction patterns and generalizability of prediction models remain conditioned on similarity in data collection and processing protocols